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This document presents a critical and comprehensive review of the available literature on the biological effects of radiofrequency (RF) radiation through 1980. The objective is to determine whether the existing data base can contribute to the formulation of RF-radiation exposure guidance for the general public.

The frequency range of concern in this document is 0.5 MHz to 100 GHz, which includes all the significant sources of population exposure to RF radiation. Research reports that are judged to be credible according to a set of objective criteria are examined for the relation between RF energy absorbed and the presence or absence of biological effects. The reported consequences of the interaction between RF radiation and biological systems are examined from four perspectives by 1) RF-energy-induced core temperature increases, 2) whole-body-averaged specific absorption rate (SAR), 3) the exogeneous energy burden as a percentage of resting metabolic rate, and 4) actual human experiences documented in epidemiological studies.

The existing data base does lead to tentative conclusions about the relation between RF-radiation exposure and biological effects that may serve as unadjusted upper limits for population exposure guidance; however, the uncertainties and unknowns in the current state of knowledge are potentially significant.

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Biological Effects of Radiofrequency Radiation

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NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the risk of existing and new man-made environmental hazards is necessary to establish sound regulatory policy. Environmental regulations enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our nation's population.

The Health Effects Research Laboratory conducts a coordinated environmental health research program in toxicology and clinical studies. These studies address problems in air pollution, radiofrequency radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory participates in the development and revision of air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is primarily responsible for providing the health basis for radiofrequency radiation guidelines. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator.

The intent of this document is to provide a comprehensive review of the scientific literature on the biological effects of radiofrequency radiation. The purpose of this effort is to evaluate critically the current state of knowledge for its pertinence and applicability in developing radiofrequency-radiation exposure guidelines for the general public.

F. G. Hueter, Ph.D.
Director
Health Effects Research Laboratory

ABSTRACT

This document presents a critical and comprehensive review of the available literature on the biological effects of radiofrequency (RF) radiation through 1980. The objective is to determine whether the existing data base can contribute to the formulation of RF-radiation exposure guidance for the general public.

The frequency range of concern in this document is 0.5 MHz to 100 GHz, which includes all the significant sources of population exposure to RF radiation. Research reports that are judged to be credible according to a set of objective criteria are examined for the relation between the RF energy absorbed and the presence or absence of biological effects. The reported consequences of the interaction between RF radiation and biological systems are examined from four perspectives by 1) RF-energy-induced core temperature increases, 2) whole-body-averaged specific absorption rate (SAR), 3) the exogeneous energy burden as a percentage of resting metabolic rate, and 4) actual human experiences documented in epidemiological studies.

The existing data base does lead to tentative conclusions about the relation between RF-radiation exposure and biological effects that may serve as unadjusted upper limits for population exposure guidance; however, the uncertainties and unknowns in the current state of knowledge are potentially significant.

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SECTION 1

INTRODUCTION

1.1 GROUND RULES AND GENERAL ASSUMPTIONS

Daniel F. Cahill

The goal and purpose of this document is to review and evaluate the available scientific information on the biological effects of radiofrequency (RF) radiation. To address this broad topic most effectively and to present the information in the most useful form, several ground rules and simplifying assumptions were adopted. It is in the selection and employment of these tools that differences of opinion are most likely to arise. These are as follows:

1. The frequency range of interest is defined as 0.5 MHz to 100 GHz. This range includes nearly all of the frequencies that serve as significant sources of population exposure (e.g., AM, FM, land mobile, and amateur radio; UHF and VHF TV; and air traffic control radar).
2. The general public is the population of concern. Therefore, far-field exposures will be the more usual condition, as compared with the near-field exposures commonly associated with the workplace. Wherever possible, the impact on all ages is considered, rather than just healthy adults, who are of principal concern in occupational exposures.
3. The concept of specific absorption rate (SAR) is used to normalize the rate of RF energy input into biological systems across this frequency range. The SAR is the mass-normalized rate at which the energy of an electromagnetic (EM) field is coupled into an absorbing body, and is reported as watts per kilogram (W/kg). Inherent in the use of a single,

whole-body-averaged SAR value is a disregard of nonuniform RF energy deposition patterns and values in excess of the average. However, the data that describe the distribution patterns of RF energy in biological systems over a frequency band as broad as 0.5 MHz to 100 GHz are far too incomplete at this time to be directly useful.

4. In reports of pulsed RF-radiation exposure experiments the time-averaged SAR is considered, although controversy exists as to whether some biological effects are functions of the temporal pattern of energy delivery or only the result of total energy input.

5. We have accepted "no effects" data in credible reports as highly valuable in our assessment of the state of knowledge in this area. These studies are considered as well as studies providing good evidence for "effects".

6. We are assuming that the human is of equal sensitivity to the experimental mammalian systems employed.

7. This document presents only the biological effects of RF radiation. The benefits of RF radiation are not considered, and therefore no benefit/risk analysis is undertaken.

1.2 GENERAL APPROACH

Although a comprehensive literature review is useful, it is even more desirable if the body of literature is consolidated, analyzed, and synthesized into a statement or statements that contribute to the definition of risk from RF-radiation exposure to the general population. To this end, our approach is essentially as follows:

1. The reports are evaluated for their scientific quality and utility. Acceptable reports contain adequate descriptions of appropriate physical and biological systems and tests.

2. The credible reports are then examined for the relation between the RF energy absorbed and the presence or absence of biological effects in the experimental systems.

3. These relations are reviewed to establish SAR levels that can be converted to equivalent power densities for humans.

1.3 SPECIFIC APPROACH USED IN THIS REVIEW

The literature evaluated for this document includes English-language publications, numerous English translations of Soviet research reports obtained through the U.S. Joint Publications Research Service, and selected technical reports translated from Polish, French, Italian, and Russian.

While the extant literature base numbers over 5000 citations, considerably fewer are valuable in developing exposure guidelines for the following reasons:

1. A significant fraction of the literature is available only in Slavic languages.
2. Biological research on RF radiation is in its formative stages compared with that on ionizing radiation and other toxicological agents, so the research reports are uneven in quality and usefulness.
3. In many review articles, equal currency is given to the conclusions from properly designed and executed studies and to those from less stringently conducted research. Because these uncritical reviews have contributed to the general confusion over the health risks associated with RF radiation, we have chosen to be highly selective in our review.

In reviewing the literature we first evaluate descriptions of frequency, exposure parameters, RF source, experimental species, age, sex, environmental and biological controls, the statistics employed, and whether actual data are displayed or merely referred to in the text. Many pre-1970 reports are deficient in one or more of these key areas and are either rejected outright if the flaws are judged fatal, or are segregated into the category of reports with "unresolved questions". Reports that provide adequate descriptions of these parameters are further scrutinized for the appropriateness of biological systems, tests, sample sizes, controls, and statistics employed, as well as substantiation of their conclusions. Those that clear this second hurdle are credible reports, but are considered usable only if biological results are linked explicitly or implicitly to SAR data from the description of the exposure parameters. Reports that fail to provide these parameters are also assigned to the "unresolved questions" category.

The reports selected for this review describe a large variety of biological effects in laboratory animals and humans exposed to RF radiation, but no assessment is made of the possible human health significance of the effects reported in animals. The reports are assessed by association with 1) induced increases of core temperature, 2) whole-body-averaged SAR, 3) SAR as a percentage increase over resting metabolic rate, and 4) the documented human experiences. Possible SAR values are determined for each of the four associations. A comparison of the SAR's is made after converting these values to equivalent power densities for humans of different ages.

SECTION 2

SUMMARY AND CONCLUSIONS

Daniel F. Cahill

Joe A. Elder

1. This document presents a critical and comprehensive review of the available literature on the biological effects of RF radiation through 1980. The objective is to determine whether the existing data base can define the relation between health risk and exposure to RF radiation.

2. RF radiation is a form of nonionizing electromagnetic radiation of very low photon energies and frequencies (0-3000 GHz), as distinguished from the very high photon energies and frequencies associated with ionizing electromagnetic radiation, e.g., x- and gamma rays. Included in the RF-radiation spectrum are AM and FM radio, UHF and VHF TV, radar, and microwave communication frequencies. The frequency range of concern in this document is 0.5 MHz to 100 GHz, which includes all the significant sources of population exposure except 60 Hz electrical power systems. However, there is little information on responses to exposure at frequencies above 10 GHz and below 10 MHz; most of the research is concentrated in the range of 900 MHz to 3 GHz.

3. RF-energy absorption by biological systems is a complex function of frequency and the dimensions, orientation, and dielectric properties of the absorber. Resonant frequencies (and their related wavelengths) for an absorber

are those at which maximum RF energy is coupled into the absorbing system. Resonance occurs when the long dimension of the absorber is approximately 0.4 times the wavelength of the incident RF radiation. The whole-body resonant frequency range for humans (from adults to infants) is approximately 30 to 300 MHz. The concept of whole-body average specific absorption rate (SAR) is used in this document to normalize the rate of energy absorption across the frequency range, 0.5 MHz to 100 GHz. SAR is the mass-normalized rate at which the energy of an electromagnetic field is coupled into an absorbing body in watts per kilogram (W/kg).

4. High level RF radiation is a source of thermal energy (e.g., microwave ovens) that carries all of the known implications of heating for biological systems. SAR's $\geq$ 3 W/kg are usually associated with increases of rectal temperature of approximately 1 °C in experimental animals. Lower SAR's can activate the heat-dissipating thermoregulatory mechanisms of the body to maintain core temperature within the normal range. The efficacy of RF radiation to activate these mechanisms increases with increasing ambient temperature and humidity, whereas the capacity to withstand high levels of RF radiation is reduced with increasing ambient temperature and humidity.

5. No consistent biological effects have yet been found with molecular and subcellular systems exposed *in vitro* to RF radiation other than those resulting from intensities that cause general temperature increases. Conclusions regarding effects of *in vitro* exposure of higher-ordered biological systems, such as single cells and brain tissue, are given below.

6. The electrophysiological properties of single cells, especially the firing rates of neurons in isolated preparations, may be affected by RF radiation in a manner different from generalized heating.

7. RF radiation does not appear to cause mutations or genetic changes in bacterial test systems unless temperatures well above the normal physiological range are produced. Similarly, no changes in chromosomes, DNA, or reproductive potential of animals have been reported in the absence of substantial rises of temperature.

8. There is a lack of convincing evidence for RF-radiation effects on the hematologic and immunologic systems without some form of thermal involvement. The reported effects of RF radiation on the hematologic and immune systems are similar to those resulting from a stress response involving the hypothalamic-hypophyseal-adrenal axis or following administration of glucocorticoids.

9. RF radiation is teratogenic at high SAR's (> 15 W/kg) that approach lethal levels for the pregnant animal. High maternal body temperatures are known to be associated with birth defects. There appears to be a threshold for the induction of experimental birth defects when a maternal rectal temperature of 41 to 42 °C is reached. Any agent capable of producing elevated internal temperatures in this range, including RF radiation, is a potential teratogen.

10. Studies involving prenatal exposure of laboratory animals to RF radiation, while few, have not shown effects on post-natal growth and development.

11. Permanent changes in reproductive efficiency have been directly associated with RF-radiation exposures that caused temperatures in animal testes greater than 45 °C. At temperatures of 37 to 42 °C mature sperm may be killed with a temporary loss of spermatogenic epithelium.

12. Neurons in the central nervous system (CNS) of experimental animals can be altered by acute, high-level and by chronic, low-level exposures (> 0.4 W/kg). The changes, which include swollen axons and decreased dendritic spines, are qualitatively similar to each other but quantitatively different and are almost always reversible. In general, pulsed RF fields produce greater changes than continuous wave sources. In addition, pulsed RF radiation may have a potentiating effect on drugs that affect nervous-system function. At present, no definitive conclusions are possible concerning RF radiation effects on the blood-brain barrier (BBB) at lower power densities (<10 mW/cm^2).

13. An increased mobilization of calcium ions occurs in brain tissue exposed *in vitro* to RF radiation, amplitude modulated at frequencies recorded in the electroencephalogram (EEG) of awake animals. The response to various intensities around 0.75 mW/cm^2 is unusual, and appears to be based on the intensity of the electric field within the tissue, that is, the SAR.

14. Some types of animal behavior are disrupted at SAR's that are approximately 25 to 50 percent of the resting metabolic rates of many species. The reported behavioral alterations appear to be reversible with time.

15. High intensity RF radiation applied to the eyes of experimental animals is cataractogenic; for single acute exposures, the threshold for cataract production exceeds 100 mW/cm^2. No cataracts have been reported in animals after whole-body, far-field RF-radiation exposures, even at near-lethal levels. The cataractogenic potential of microwaves varies with frequency; the most effective frequencies appear to be in the 1 to 10 GHz range. Similar ocular effects are produced by both CW and pulsed RF radiation of the same average intensity.

16. Pulsed RF radiation in the range 216 to 6500 MHz has been heard by some human beings. The sound associated with the "RF hearing" varies with pulse width and pulse-repetition rate and is described as a click, buzz, or chirp. The threshold for human perception of this effect is approximately 40 $\mu J/cm^2$ (incident energy density per pulse). The most generally accepted mechanism for the RF-auditory sensation is that the incident pulse induces a minuscule but rapid thermoelastic expansion within the skull, resulting in an acoustic pressure wave that is conducted by the bone to the cochlear region of the ear.

17. Cutaneous perception of heat and pain is an unreliable sensory mechanism for protection against potentially harmful RF-radiation exposure levels. Many frequencies deposit most of their energy at depths below the cutaneous thermal receptors.

18. Changes reported in endocrine gland function and blood chemistry are similar to those observed during heat stress and are generally associated with SAR's > 1 W/kg. Exposures of sufficient intensity to produce whole body heating will produce an increase in heart rate similar to that caused by heating from other sources. Changes in whole body metabolism have been reported following exposures at thermal levels (~ 10 W/kg), while brain energy metabolism is altered at levels as low as 0.1 W/kg following irradiation of the exposed surface of the brain of anesthesized animals.

19. RF-radiation exposures below acute lethal levels do not appear to have any carcinogenic or life shortening potential in experimental animals.

20. Human data are currently limited and incomplete but do not indicate any obvious relationship between prolonged low level RF-radiation exposure and increased mortality or morbidity, including cancer incidence.

21. The development of population exposure guidelines necessitates that the consequences of the interaction between RF radiation and biological systems be quantified in some manner. Four possible approaches are considered here, namely, 1) whole-body-average SAR, 2) the exogenous energy burden as a percentage of resting metabolic rate (RMR), 3) RF-energy-induced core temperature increases, and 4) the actual human experiences documented in epidemiological studies. No one relationship is entirely adequate for estimating population exposure guidelines. However, the available data base viewed from each of these four perspectives can contribute some insights about population exposure guidelines, as detailed below:

a. Approximately 75 percent of the studies that met the criteria for acceptability in this document employed SAR's < 10 W/kg. Virtually all of the "no effects" data are associated with SAR's < 6 W/kg. Thus, "effects" are highly likely at > 6 W/kg. Below 6 W/kg nearly 90 percent of the "effects" reported involve behavior, CNS structure, hematologic/immunologic, or hormonal end points; of these, behavioral and hematologic/immunologic changes predominate. Despite the recognizably incomplete state of knowledge in this area, the currently available information suggests that the biologically effective SAR for mammalian systems lies in the range 0.4 to 6.0 W/kg.

b. An inverse linear correlation appears to exist between the log of body mass for several mammalian species and the log of the SAR required to activate a physiological, thermoregulatory response. For humans this "activation" point would be approximately 25 percent of the RMR for all ages, or approximately 0.27 to 0.81 W/kg.

c. In humans, a core temperature rise of 0.5 °C is within the normal range of daily fluctuations and less than the 1 °C rise permitted for occupational heat stress. RF-radiation-induced, transient core temperature increases of < 0.5 °C could be roximations of population exposure guidelines. No experimental data are available to provide the SAR necessary to induce this temperature rise in humans; however, mathematical models predict that an SAR of approximately 1.4 W/kg would be required.

d. As stated above, human data are limited and incomplete but do not indicate any obvious relationship between low level RF-radiation exposure and increased mortality or morbidity.

22. While existing data lead to tentative conclusions about the relation between RF-radiation exposure and biological effects, the unknowns are potentially significant in attempting to establish exposure guidance. These unknowns include a lack of knowledge of 1) effects of most frequencies in the range 0.5 MHz to 100 GHz; 2) effects of chronic, low-level exposures on human beings and laboratory animals; 3) the most sensitive segment(s) of the population; 4) the influence of ambient environmental conditions and of potential synergistic interaction with other agents; 5) the implication of nonhomogeneous

RF-energy deposition; 6) the existence and significance of frequency-specific effects and power density windows; and 7) the physical mechanisms of interaction at low exposure levels. Given our present, limited knowledge of the health effects of RF-radiation exposure, the prospects for revision and refinement of the summary statements and conclusions stated above are considerable.

SECTION 3

PHYSICAL PRINCIPLES OF ELECTROMAGNETIC FIELD INTERACTIONS

3.1 ELECTROMAGNETIC FIELD THEORY

William T. Joines

3.1.1 Electromagnetic Spectrum

3.1.1.1 Frequency, Wavelength, and Velocity--

Oscillating electric charges induce an electromagnetic (EM) field within the region surrounding the charge source. In turn, this oscillating induction field--often called the near field--of the source generates an EM wave that radiates energy from the region surrounding the charges. The radiated wave consists of coupled electric and magnetic fields that oscillate at the same frequency as the source, and the wave propagates outward from the source at the velocity of light in the medium. In a vacuum or free space, this is $\sim 3 \times 10^8$ m/s, whereas in a medium with low EM energy dissipation this value is divided by the square root of the material's dielectric constant relative to that of free space. In a low-loss material such as fatty tissue, with a relative dielectric constant of 4, the velocity of light is 1.5×10^8 m/s. For an EM wave traveling at velocity v, the wavelength in the medium is the distance the wave travels in one time period or $T = 1/f$, where f is the oscillation frequency of the wave in cycles per second, or hertz (Hz). Therefore, the wavelength λ is expressed as

$$\lambda = v/f$$

The EM spectrum extends from zero to 10^{25} Hz (or cycles/s) and includes the ranges of visible light and ultraviolet (UV), infrared (IR), x-, and gamma rays. The region from zero to 3000 GHz (lower IR range) is referred to as the RF region (Sams & Co. 1981). The region of interest here is the RF band from 0.5 MHz to 100 GHz. The wavelengths in free space for this frequency band range from 1000 m to 7.5 mm.

3.1.1.2 Ionizing and Nonionizing Electromagnetic Radiation--

EM waves of all frequencies carry energy. According to quantum mechanics, they can also be thought of as packets of energy called photons. The energy of a photon is given by

$$\text{Energy} = hf$$

where $h = 6.63 \times 10^{-34}$ joule seconds (Planck's constant)

f = frequency

We see from the above equation that the energy of a photon is directly proportional to the frequency of the radiation. When the frequency approaches or exceeds 3×10^{15} Hz (UV), the photon energies equal or exceed 2×10^{-18} J, or 12.4 eV, and become comparable to the binding energy of electrons to atoms. This high-frequency radiation (x-rays, gamma rays, etc.) is referred to as ionizing radiation. Since even the weakest chemical bonds have energies that are several orders of magnitude greater than those of RF or microwave photons (10^{-3} eV or less), RF waves are referred to as nonionizing radiation.

3.1.1.3 Designation of Microwave and Radiofrequency Bands--

Bands of radiofrequencies have been assigned designations according to frequency or wavelength as shown in Table 3-1 (Sams & Co. 1981). Typical uses of the frequencies within a band are also indicated. Certain radiofrequencies--notably the industrial, scientific, and medical (ISM) frequencies--have been assigned by the Federal Communications Commission (Sams & Co. 1981) for specific applications. The ISM frequencies are

13.56 MHz ± 6.78 kHz
27.12 MHz ± 160 kHz
40.68 MHz ± 20 kHz
915 MHz ± 25 MHz
2450 MHz ± 50 MHz
5800 MHz ± 75 MHz
22,125 MHz ± 125 MHz

TABLE 3-1. RADIOFREQUENCY BANDS*

Frequency	Wavelength	Band Designation	Typical Uses
300-3000 GHz	1-0.1 mm	Supra EHF (extremely high frequency)	Not allocated
30-300 GHz	10-1 mm	Extremely high frequency (EHF)	Satellite communications, radar, microwave relay, radionavigation, amateur radio
3-30 GHz	10-1 cm	Super high frequency (SHF)	Satellite communications, radar, amateur, microwave relay, airborne weather radar, ISM
0.3-3 GHz	100-10 cm	Ultra high frequency (UHF)	Microwave point to point, amateur, taxi, police, fire radar, citizens band, radionavigation, UHF-TV, microwave ovens, medical diathermy, ISM
30-300 MHz	10-1 m	Very high frequency (VHF)	Police, fire, amateur FM, VHF-TV, industrial RF equipment diathermy, emergency medical radio, air traffic control
3-30 MHz	100-10 m	High frequency (HF)	Citizens band, amateur, medical diathermy, Voice of America, broadcast, International Communications, industrial RF equipment
0.3-3 MHz	10^3-10^2 m	Medium frequency (MF)	Communications, radionavigation, marine radiophone, amateur, industrial RF equipment, AM broadcast
30-300 kHz	10-1 km	Low frequency (LF)	Radionavigation, marine communications, long range communications
3-30 kHz	100-10 km	Very low frequency (VLF)	Very long range communications, audiofrequencies, navigation
0.3-3 kHz	10^3-10^2 km	Voice frequency (VF)	Voice, audiofrequencies
30-300 Hz	10^4-10^3 km	Extremely low frequency (ELF)	Power lines, audiofrequencies, submarine communications
0-30 Hz	∞-10^4 km	Sub-ELF	Direct current power lines

*Sams & Co. 1981.

3.1.2 Wave Propagation

Power Density, Electric Field, and Magnetic Field--

In free space, EM waves spread uniformly in all directions from a theoretical point source. The wavefront, or the surface joining all points of identical phase, is spherical in this case. As the distance from the point source increases, the area of the wavefront surface increases as a square of the distance, thus spreading the source power over a larger area. If power density is defined as the ratio of the total radiated power to the spherical surface area enclosing the source, the power density W is inversely proportional to the square of the distance from the source, and can be expressed as

$$W = P/4\pi r^2 \tag{3-1}$$

where P = transmitted power

r = distance from the source

An isotropic source radiates uniformly in all directions in space. In practice, there is no source having this property, although there are close approximations. The inverse-square law (Equation 3-1) applies also when the source is anisotropic (directional), as long as the medium is homogeneous and isotropic (e.g., free space or a medium in which the velocity of wave propagation does not change with distance).

An EM wave is also characterized by its electric-field (E) intensity and its magnetic-field (H) intensity. In a medium not bounded by conductors, the product of E and H is the power density W, or

$$W = EH \qquad (3\text{-}2)$$

where E is in volts per meter, H is in amperes per meter, and W is in watts per square meter. The ratio of E to H is the intrinsic impedance of the medium η (in ohms), or

$$\eta = E/H \qquad (3\text{-}3)$$

where η is $120\pi\ \Omega$ in free space (or vacuum). Using Equations 3-1 through 3-3, it is possible to express E in free space at a distance r from an isotropic source radiating total power P as

$$E = \sqrt{30\ P}/r \qquad (3\text{-}4)$$

The radiated waves that propagate outward from an RF or microwave source can be confined to travel along a two-conductor transmission line (coaxial, stripline, microstrip, twin lead), or inside a hollow metal pipe (waveguide). The waves can also be propagated outward into the space that surrounds a transmitting antenna, as in communications broadcasting. In this case, the RF or microwave source forces electrons to oscillate on the surface of a metal-transmitting antenna, thereby producing EM waves. This is a reciprocal process, for when these waves strike a receiving antenna, they force electrons to oscillate. This commutative phenomenon forms the basis of EM communication systems. Information can be placed on an EM carrier in several ways, including by impression of amplitude and frequency modulation.

3.1.2.1 Sources of Radiofrequency Radiation--

There is a widespread interest in possible new applications of RF energy, especially at microwave frequencies. The growing number of commercial applications has led to an increased awareness of potential hazards due to the energy sources used. Typical sources of RF or microwave energy are klystrons, magnetrons, planar triodes, backward-wave oscillators, and semiconductor devices. In all of these sources, energy is imparted to charged particles or electrons from a convenient supply, usually a direct voltage or current. A portion of the energy is then given up by the charged particles in the form of oscillations in a tuned circuit. Such sources may operate to produce (1) continuous (CW) radiation, as in the case of some communications systems; (2) intermittently, as in microwave ovens, induction heating equipment, and diathermy equipment; or (3) in the pulsed (PW) mode in radar systems.

3.1.2.2 Plane-Wave, Far-Field, and Near-Field Concepts--

Usually the region that is more than a few wavelengths from the transmitting antenna is called the far field. In this region, the spatial relationship between the electric and magnetic fields in the EM wave is that shown in Figure 3-1. In this diagram, an EM wave is propagating in a direction perpendicular to the motion of the electrons in the transmitting antenna. The electric field E is always perpendicular to the direction of propagation and

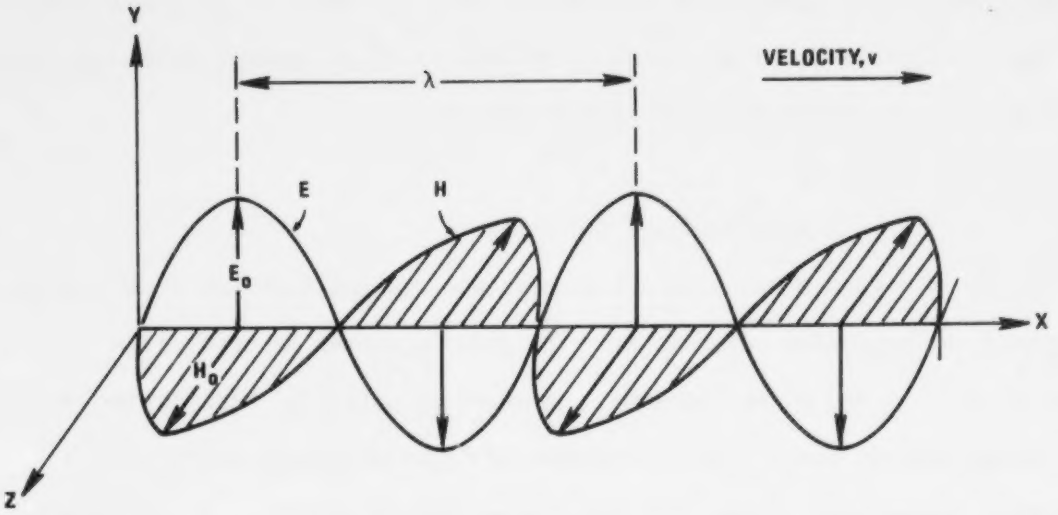

Figure 3-1. Far-field electromagnetic wave at a particular instant in time.

lies in the plane formed by the line of propagation and the motion of electrons in the antenna. The direction of the electric vector periodically changes along the direction of propagation, and its magnitude forms a sine-wave function. The magnetic field H, which is always perpendicular to both the electric field E and the line of propagation, traces out a sine-wave function in the same manner as the electric field E. Figure 3-1 depicts the situation at a particular instant in time. The entire wave can be pictured as moving along the line of propagation at $\sim 3 \times 10^8$ m/s.

At distances less than a few wavelengths from a transmitting antenna, in the near field, the situation is somewhat complicated because the maxima and minima of E and H do not occur at the same points along the direction of propagation as they do in the far-field case (Figure 3-1). Near-field exposures become particularly important when one is considering radiation from microwave ovens, microwave diathermy equipment, RF sealers, broadcast antennas, and microwave oscillators under test. For investigations into the biological effects of RF-radiation exposure, studies of exposures in the far field are usually preferable; field strengths in the near field are more difficult to specify because both E and H must be measured and because the field patterns are more complicated.

Incident power density at a point in front of an antenna may be calculated from the measured power transmitted by the antenna, the known antenna gain G, and effective area A of the antenna. Antenna gain is defined as the power density at a point in front of the antenna divided by the power density at the same point if the antenna were radiating the same total power as an isotropic source. For any impedance-matched antenna (i.e., one where all the energy fed to it is transmitted), the ratio of G to A is

$$G/A = 4\pi/\lambda^2 \tag{3-5}$$

The far-field power density is calculated from the Friis free-space transmission formula (Mumford 1961) as

$$W = GP/4\pi r^2 = AP/\lambda^2 r^2 \tag{3-6}$$

where λ = wavelength

P = power output of the antenna

W = power density on a surface at distance r from the antenna

It is convenient to express the far-field free-space power density in terms of the power density at the antenna aperture, i.e., $W_0 = P/A$, and hence $P = W_0A$. Substituting this expression for P in Equation 3-6 and dividing both sides by W_0 yields

$$W/W_0 = (A/\lambda r)^2 \tag{3-7}$$

Equation 3-7 may be rewritten as

$$W/W_0 = 4(A/2\lambda r)^2 \tag{3-8}$$

This expression applies in the far-field region, and the following simple modification makes it applicable to the near-field region as well

$$W/W_0 = 4\sin^2(A/2\lambda r) \tag{3-9}$$

This formula applies to uniform irradiation of square, round, or rectangular apertures or to irradiation that is tapered in amplitude for round apertures. For other shapes and tapers, a more complicated analysis is necessary (Mumford 1961).

Since the power density at the antenna aperture ($W_0 = P/A$) is greater than the output power P divided by the cross-sectional area of the aperture, the effective area A is less than the actual area. For the waveguide horn and dish antennas commonly used at microwave frequencies, the effective area ranges from about 50 to 80 percent of the actual area of the cross-section.

For a given P, with A determined for the particular antenna used, $W_0 = P/A$ is used in Equation 3-9 to compute W at any distance r from the antenna (Mumford 1961).

Equation 3-9 is plotted in Figure 3-2 along with lines representing the maximum values in the near-field and the far-field approximations as given by Equation 3-7. In this graph, the relative power density is plotted in decibels $[\mathrm{dB} = 10\log_{10}(W/W_0)]$ on the ordinate, and $\lambda r/A$ is plotted logarithmically on the abscissa. Note the alternate maxima and minima in the near field. The maxima all are 6 dB above (4 times) the power density at the aperture. To be conservative in possible near-field human exposure situations, the power density can be approximated as the maximum value or

$$W = 4W_0 = 4P/A \qquad (3\text{-}10)$$

Note, also, from Figure 3-2 and Equation 3-9 that for $\lambda r/A = 1$, $W \cong W_0$, the power density at the antenna aperture. Hence, a convenient point of demarcation between the near field and far field is the distance from the antenna where

$$r = A/\lambda \qquad (3\text{-}11)$$

3.1.3 Wave Modulation

3.1.3.1 Amplitude and Frequency Modulation--

With an EM wave of a particular frequency serving as a carrier, information signals at lower frequencies are translated onto the carrier through

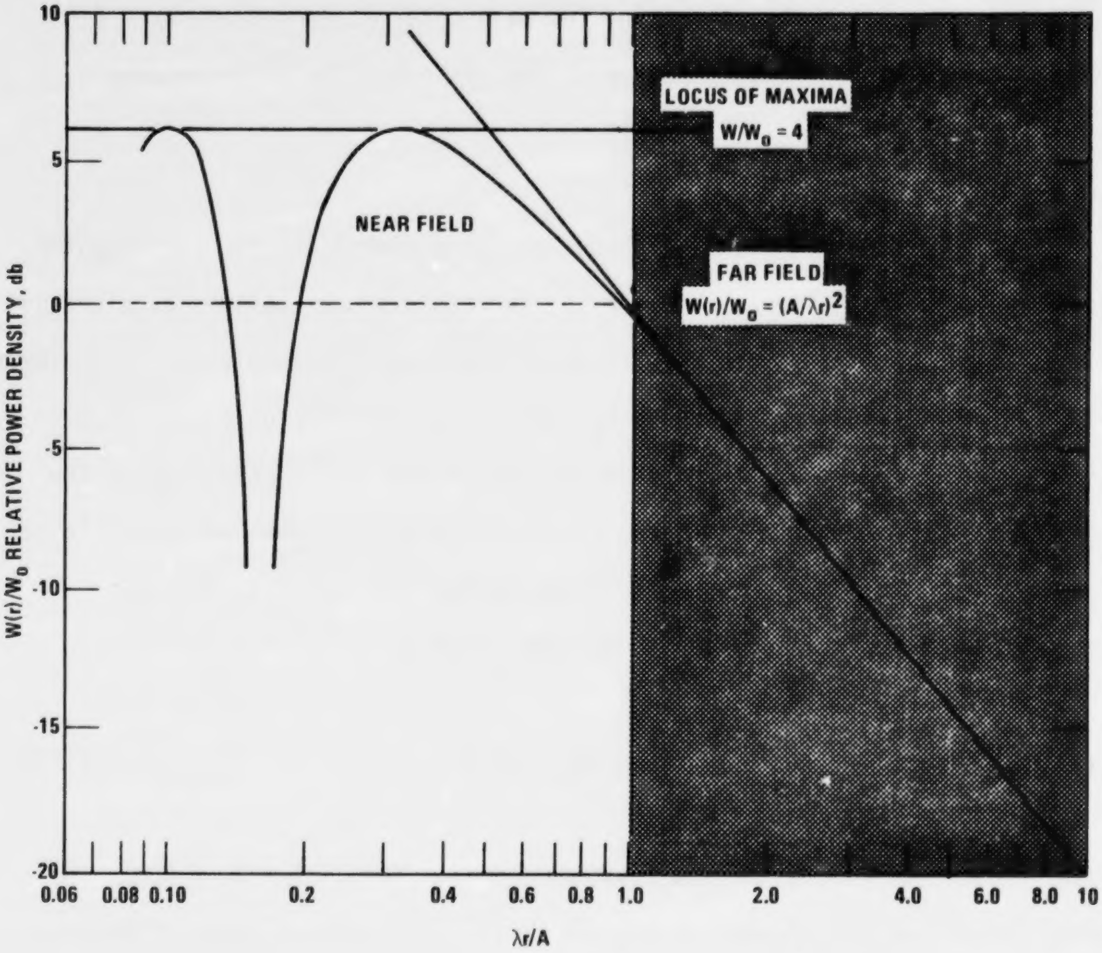

Figure 3-2. Power density vs. distance along axis from antenna aperture.

the process of modulation. Modulation of the carrier can be accomplished either by continuously varying one of the parameters of the carrier (amplitude, frequency, or phase) or by interrupting the carrier by chopping it into segments (PW modulation). If the impression of the information signal on the carrier causes its amplitude to vary, the process is called amplitude modulation (AM). If the information signal causes a frequency variation of the carrier, the process is called frequency modulation (FM). If the information signal causes a time-phase variation of the carrier, the process is called phase modulation (PM). Phase modulation and frequency modulation are closely related; both cause a change in the time phase angle of the carrier (Froehlich 1969).

Since the purpose of modulation is to improve the overall efficiency of transmission, the carrier frequency is chosen for its suitability to the medium in which it is to be transmitted. Transmitting unmodified audio signals is theoretically possible; however, the antenna required to transmit and receive such signals is extremely large and impractical. More importantly, unmodulated signals are not transmitted because no other method exists to separate several information signals on the same transmission path to provide for multi-channel capability. This flexibility is obtained if carriers of higher frequencies are chosen and then spaced in frequency so as to prevent overlapping. High-frequency carriers are also more suitable for radio propagation. It, therefore, becomes necessary to shift the information signal to a high-frequency range through the process of modulation. Introducing frequency translation to information signals provides a way to separate information channels and thereby improve the transmission efficiency.

3.1.3.2 Pulse Modulation--

One of the more familiar applications of PW modulation is in radar. Radar is possible because EM waves at some frequencies are reflected by certain materials, including water vapor in clouds and metal surfaces. A radar antenna can transmit and receive and is directional; that is, it transmits and receives signals in a limited direction. For most purposes, the radar antenna sends out short pulses of EM waves and later receives the reflected pulses. The radar system determines the time that elapses between the departure of the outgoing pulse and the arrival of the incoming pulse and correlates this elapsed time with the antenna's direction of propagation. This information is then used to pinpoint accurately the position of the reflecting objects, such as airplanes or cloud formations. The magnitude of the incoming reflected pulse is smaller than the outgoing pulse by a factor of millions and sometimes billions. To detect an incoming pulse in the presence of atmospheric noise, the power of the outgoing pulse is often made as large as possible.

The duty factor (DF) of a transmitter is the ratio of the pulse width of the transmitted RF to the time between the leading edge of consecutive pulses. Hence, average power (P_{av}) is determined from peak power (P_{peak}) by

$$P_{av} = (DF)P_{peak}$$

In general, long-range radars have a larger transmitted pulse power and a longer waiting time between pulses (lower DF) than do short-range radars. For this reason, long-range and short-range radars may have exactly the same average transmitted power.

3.2 RF-FIELD INTERACTIONS WITH BIOLOGICAL SYSTEMS

Claude M. Weil
James R. Rabinowitz

Consideration of the coupling of RF radiation into different biological objects (human, animal, bird, etc.) is important to any study of the biological effects of RF-radiation exposure. From measurements and predictions of RF-energy absorption that are based on experimentation with lower animals, one can extrapolate data for estimating effects of RF radiation on humans. Furthermore, an adequate understanding of the interaction of RF radiation with humans has been crucial in determining exposure limits recommended in the American National Standards Institute (ANSI) C95.1 standard (ANSI 1982). The 1982 ANSI guideline essentially is based on the concept of a defined, maximum whole-body exogeneous heat load (see § 4). Consequently, relating this quantity to a maximum permissible incident power density requires an in-depth understanding of the RF energy-human interaction.

3.2.1 Scattering and Absorption of Electromagnetic Waves

The interaction of EM waves with any irradiated object is a complex event, the study of which forms a large part of electromagnetism. When an EM wave propagating in air impinges normally on any material having dielectric properties different from those of air, a reflected wave, created at the air-dielectric interface, propagates in a direction opposite to that of the incident wave. This interaction is illustrated in Figure 3-3 for three materials of differing electrical properties. At the top of the figure, an EM wave is

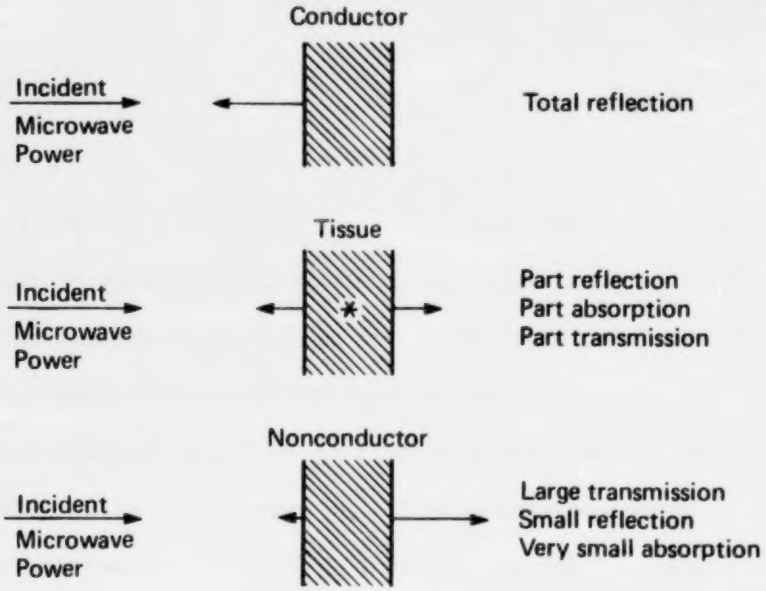
Conductor
Incident
Microwave
Power
Total reflection
Tissue
Incident
Microwave
Power
Part reflection
Part absorption
Part transmission
Nonconductor
Incident
Microwave
Power
Large transmission
Small reflection
Very small absorption

Figure 3-3. Interaction of RF radiation with electrical conductors, biological tissue, and electrical insulators (Sher 1970).

shown incident on a metallic conductor. In this case, virtually all of the incident energy is reflected back to its source by the conductive plate. At the bottom of the figure, the energy is shown incident on a slab of low-loss, nonconductive material (dielectric insulator) where almost no energy is dissipated within the material. For the case with nonconductive material, most incident energy is transmitted through the slab to the other side with a small amount reflected back at the first air-dielectric interface. Because this material exhibits almost no dielectric losses, it absorbs very little of the incident radiation. The third case, shown in the middle of Figure 3-3, illustrates the interaction of an incident wave with a slab of what is termed a complex dielectric. All biological tissues fall into this category. The electrical properties of a complex dielectric would place it roughly between the conductor and the nonconductor in Figure 3-3; i.e., it exhibits values of relative permittivity (a measure of how strongly the material reflects energy) and conductivity (how well the material conducts electrically) that fall between the very high values for a metallic conductor and the near-zero values for a dielectric insulator. For this reason, part of the energy incident on the slab of complex dielectric shown in the center of Figure 3-3 is reflected, part is absorbed by the tissue medium, and part is transmitted. If the tissue slab is of sufficient thickness, all incident energy will either be reflected or absorbed, and there will be no energy transmitted through the slab. The mechanism by which RF energy is absorbed or dissipated within the tissue slab is discussed in more detail below.

The reflected and transmitted waves that surround a dielectric object irradiated by an incident RF wave together comprise what is termed the scattered field. Scattering by a dielectric object plus absorption within the object, where applicable, represent the two basic components of the EM interaction phenomenon. The degree to which any object interacts with an EM field when irradiated by a uniform plane wave is defined in terms of scattering and absorption cross sections. These represent the cross-sectional area in square meters of an equivalent flat plate placed normal to the direction of propagation, which will either totally reflect (in the case of the scattering cross section) or totally absorb (in the case of the absorption cross section) the radiant energy incident on the plate.

In general, the EM cross section is smaller than the geometric or optical cross section that the object creates when illuminated by a distant light source. However, under certain conditions--termed resonance--when the wavelength of the incident radiation is comparable to the physical dimensions of the object, the scattering and absorption effects become enhanced, such that both respective cross sections exceed the geometric cross section. Resonance is a significant phenomenon that will be discussed in more detail in the following sections; it can be explained by the apparent ability of the resonant object to intercept or "pull in" considerably more of the energy incident upon it relative to the optical case.

The terms "scattering coefficient" and "absorption coefficient," referring to measures of the efficiency with which an object scatters and absorbs energy, are defined as the ratio of the scattering-to-optical cross sections and the absorption-to-optical cross sections, respectively. Of the two basic measures of interaction, the absorption coefficient is considerably more important when discussing the interaction of EM waves with biological bodies. This is because any potentially adverse biological effects are related to the energy that the body is absorbing, and not to what is scattered. For this reason, most of the remaining material in this section deals only with the absorptive aspect of the interaction phenomenon.

Some measurements have been made of the scattered fields that surround both human subjects and life-size phantom models exposed to incident microwave fields (Reno 1974). Although this work illustrates well the complex scattered fields surrounding the irradiated subject (see Figure 3-4), no attempts have

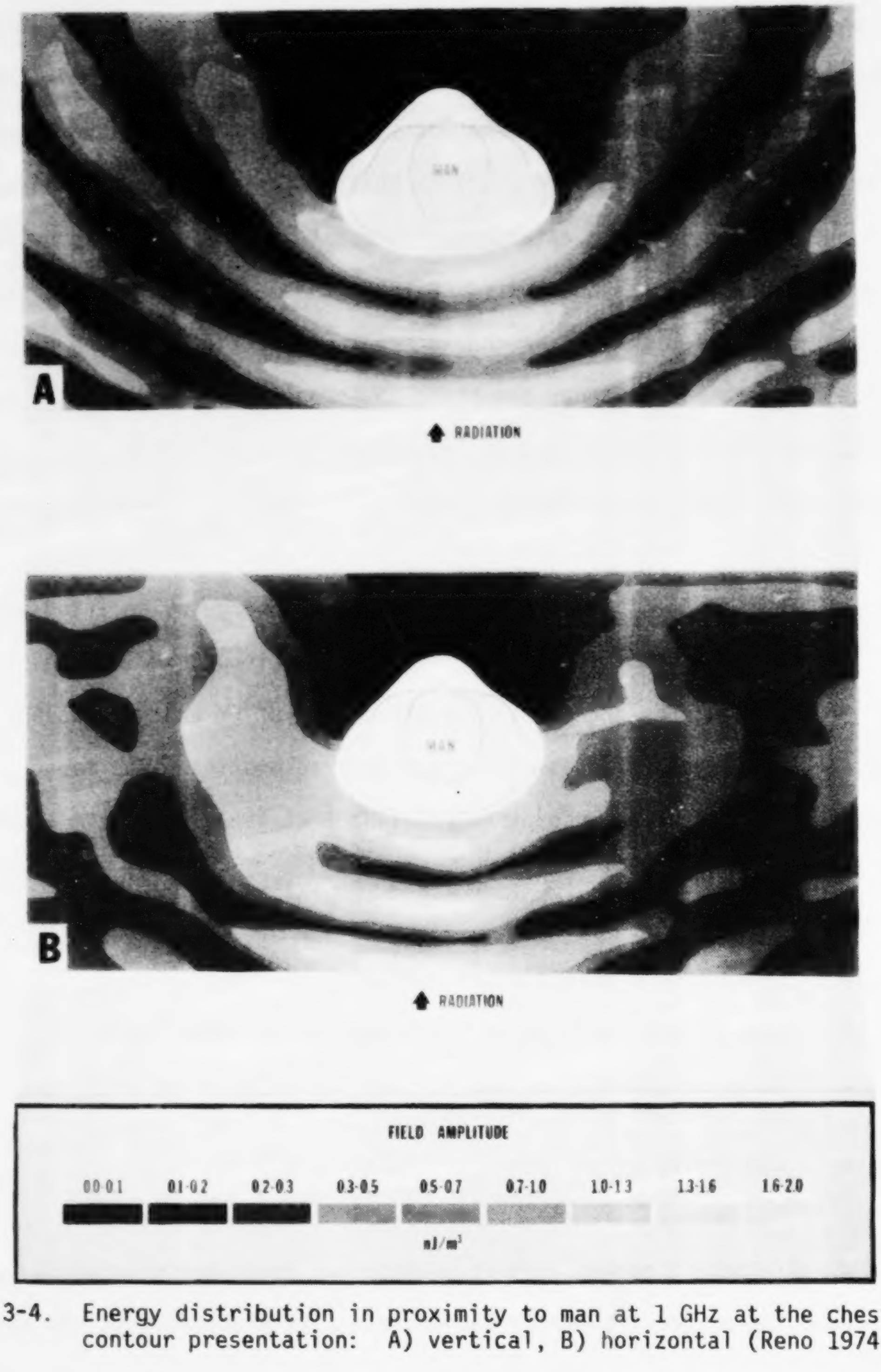

Figure 3-4. Energy distribution in proximity to man at 1 GHz at the chest plane contour presentation: A) vertical, B) horizontal (Reno 1974).

yet been made to relate the field patterns to what the subject is absorbing. Although it is theoretically possible to determine the energy being absorbed and the internal distribution from measurements of the distribution of externally scattered fields, in practice this determination remains a difficult task and has not yet been attempted. Interest in this area is growing, as evidenced by a recent symposium (IEEE 1980) that addressed methods of obtaining high-resolution imagery of the internal dielectric structure of a biological target. The methods are based on techniques of probing the scattered fields created when the target is irradiated by an RF field. The scope for future work in this area appears large, particularly in diagnostic applications.

3.2.1.1 Factors Affecting the Absorption of RF Energy by an Irradiated Subject--

The greater the degree of interaction of an irradiated biological subject with an EM field, the greater is the efficiency of EM energy coupling into the body, and the greater the overall whole-body absorption. The factors influencing the degree of absorptive coupling that takes place are listed below and will be discussed in turn:

a. Dielectric composition of subject
b. Object size relative to wavelength of incident field
c. Shape or geometry of subject and its orientation with respect to polarization of incident field
d. Complexity of incident radiation

a. Dielectric composition of subject--As mentioned previously, absorptive coupling to the irradiated subject can take place only if the subject is composed of dissipative dielectrics having a finite conductivity value. The dielectric properties of all biological tissues fall into this category, primarily because their major constituent is water (average of 70 to 80 percent by mass), which contains electrically polarizable or dipolar molecules as well as free ions. The basic mechanism of dissipation of incident RF energy within these tissues is that 1) the free rotations induced in the dipolar water molecules by the externally impressed electric field are damped out by collisions with surrounding molecules, and 2) conduction currents are induced within the tissue medium because of the presence of free ions. These phenomena are discussed extensively in § 3.2.4, Mechanisms of RF Interaction with Biological Systems.

Over the past 40 years, many measurements have been made of the dielectric properties of biological tissues. These data have been collected in the Radiofrequency Radiation Dosimetry Handbook (Durney et al. 1978, Tables 9 and 10) as well as in a more recent paper by Stuchly and Stuchly (1980). The dielectric properties of biological tissues depend to a considerable extent on the water content of the tissue; i.e., tissues of high water content (blood, skin, muscle, brain, etc.) exhibit much higher permittivity and conductivity values than do tissues of low water content (fat, bone, etc.). As a result, most incident RF energy will tend to pass through the fatty surface tissues of the body and be deposited in the deeper tissues such as muscle and brain. Figure 3-5 illustrates some dielectric data for different types of tissues in the RF range 0.01 to 10 GHz. Note that the dielectric properties of tissue are not constant, but change with frequency. This is an example of what is termed a dispersive dielectric. For the case of biological tissues, the dispersive

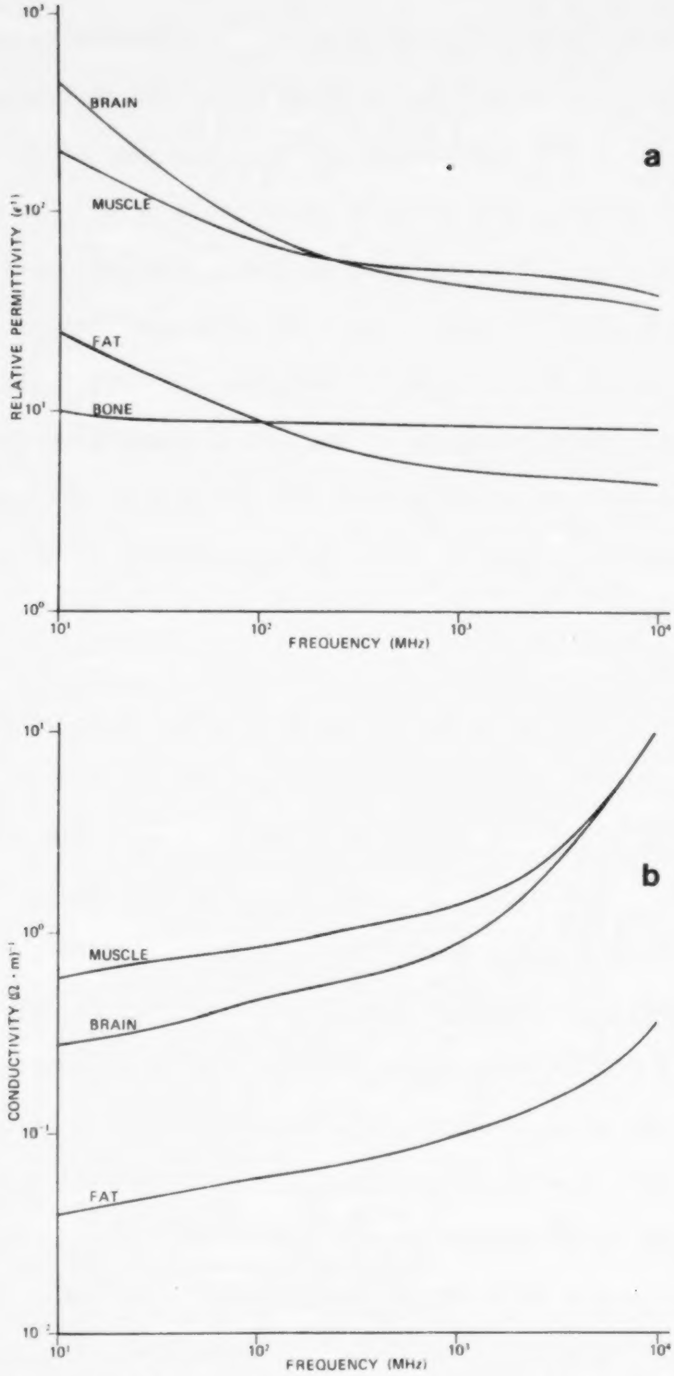

Figure 3-5. Dielectric data for tissues in RF range 0.01 to 10 GHz. a: permittivity, b: conductivity.

characteristic above 1 GHz is created by the Debye relaxation phenomenon in water molecules (discussed further in § 3.2.4, Mechanisms of RF Interaction with Biological Systems). In part b of Figure 3-5, it is apparent that conductivity increases by almost an order of magnitude for all tissues in the frequency range from 1 to 10 GHz. Because of this fundamental dielectric property of tissue, microwaves in the frequency range above about 5 GHz become strongly attenuated in the increasingly lossy tissue medium. Consequently, microwave energy of such frequencies is unable to penetrate deeply into body tissues and is deposited near the body surface. As a result of their poor penetration capability, microwaves in the centimetric wavelength region ($\leq$ 6 cm approximately) are less capable of inflicting potential damage on internal tissue than are those of longer wavelength ($\geq$ 10 cm).

b. Object size relative to wavelength of incident field--The second major factor upon which energy absorption depends is the size of the irradiated object relative to the wavelength of the incident radiation. Figure 3-6 illustrates that when the wavelength is much greater than the object size (see case A at top of figure), the absorptive coupling is inefficient and the object is almost transparent to the radiation; i.e., little energy is deposited in the object. For this case, values of the absorption coefficient lie in the range 0 to 0.5, and the case is referred to as the subresonant condition. Case B illustrates the resonant case, which occurs when the wavelength and object dimensions are of comparable size. For this case, the absorptive efficiency is markedly improved so that significantly more RF energy is coupled into the object, creating much greater deposition. Absorption coefficient values in the range 1.5 to 4 are obtained under resonant

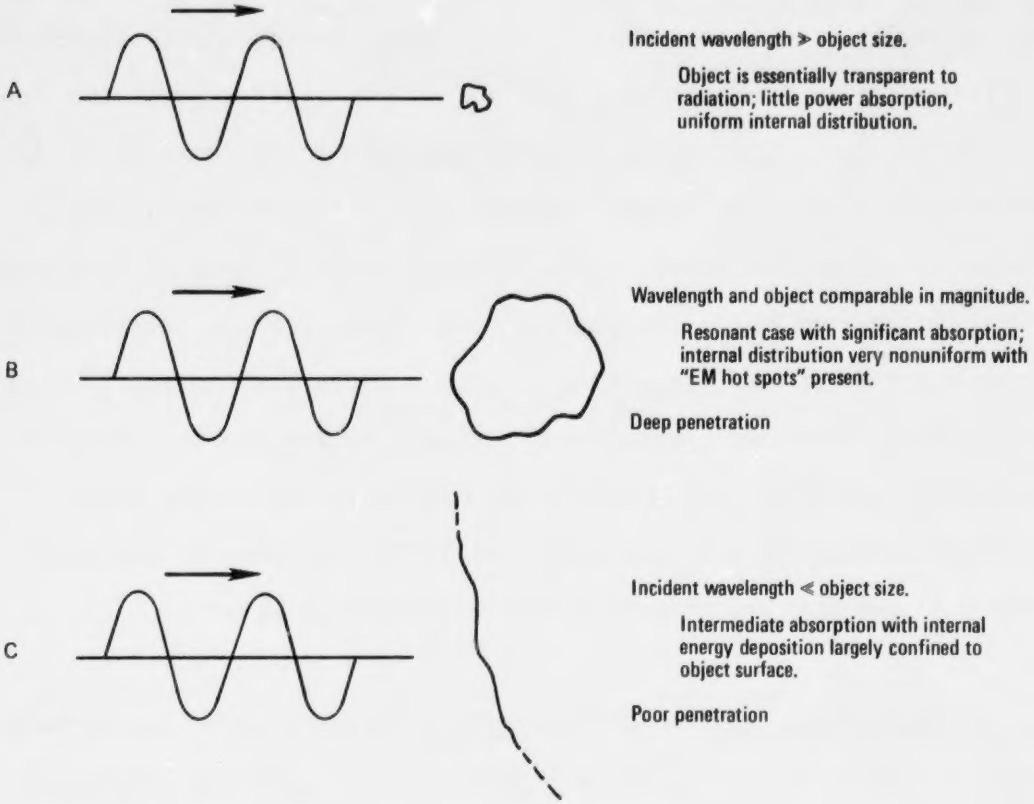
A
Incident wavelength ≫ object size.
Object is essentially transparent to radiation; little power absorption, uniform internal distribution.
B
Wavelength and object comparable in magnitude.
Resonant case with significant absorption; internal distribution very nonuniform with "EM hot spots" present.
Deep penetration
C
Incident wavelength ≪ object size.
Intermediate absorption with internal energy deposition largely confined to object surface.
Poor penetration

Figure 3-6. Illustration of object size vs. wavelength dependence. (Object is composed of tissue-like dispersive dielectric.)

conditions. Furthermore, the incident energy penetrates deeply into the object and is deposited internally in a characteristically nonuniform manner, creating localized regions of enhanced energy deposition ("EM hot spots") at or near the object's center. These effects are discussed further in later sections of this document. In case c shown at the bottom of Figure 3-6, the wavelength is much shorter than the object size. This represents the quasi-optical case, where the absorptive efficiency is similar

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to that occurring at optical wavelengths. The absorption coefficient approaches ~ 0.5 under these conditions, which gives intermediate absorption values that fall between those achieved with the conditions of cases A and B. Case C is also characterized by the inability of the incident energy to penetrate much beyond the surface of the object (please refer to the dielectric factors discussed earlier); consequently, the energy coupled into the object under these conditions is confined to the object surface.

c. Geometry and orientation of subject--The third factor upon which energy absorption depends is the shape of the object and its orientation with respect to the electric-field vector of the incident field. Most biological subjects used in studying the biological effects of RF radiation have a characteristic shape that is significantly elongated along one axis (similarly to humans). Although this observation may appear to be simplistic, it is of considerable significance when discussing the interaction of RF waves with such objects. When the electric-field vector of the incident radiation is oriented parallel to the major or long axis of the irradiated subject (e.g., a vertically polarized field that is incident on a standing human subject), then the subject will absorb as much as ten times more energy at resonance than if the electric-field vector is oriented parallel to either of the two minor axes. Figure 3-7 illustrates a prolate spheroidal model of an average human. The ordinate represents the whole-body-averaged specific absorption rate (SAR), (see § 3.2.2, RF Dosimetry Definitions, for discussion of units), and the abscissa represents frequency. From Figure 3-7, it is evident that when the electric-field vector is oriented parallel to the long axis of the prolate spheroid (electric-field polarization case), the absorption curve has a sharp

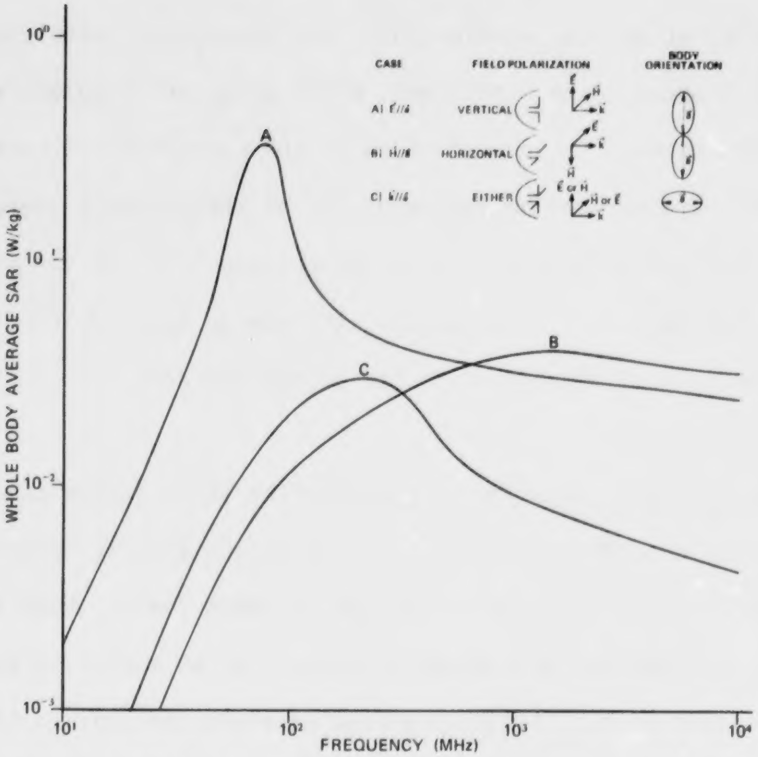


Figure 3-7. Whole-body average SAR vs. frequency for three polarizations in a prolate spheroidal model of a human; incident power density = 1 mW/cm^2.

peak at the resonant frequency of ~ 80 MHz. For the other orientations (H- and k- polarization cases), it is apparent that the absorption peak is much broader and occurs at somewhat higher frequencies. Furthermore, the resonant absorption values for the H and k cases are considerably lower than that for the E polarization case. Note that these basic differences in absorption values hold true in both the subresonant and resonant regions, but no longer hold in the above-resonant (or quasi-optical) region, where absorption in the E- and H-polarization cases is approximately equal.

d. Complexity of incident radiation--The fourth and final factor upon which RF-energy absorption depends involves the complexity of the incident radiation. Up to this point, most of the discussions of RF coupling in biological tragets have assumed the simplest form of free-field exposure, which involves a unipath plane wave emanating from a distant source and incident on a subject suspended in space. Virtually all of the RF-radiation protection guides and standards in use throughout the world are based on this rather idealized assumption. Furthermore, most of the biological experimentation involving free-field exposures in anechoic chambers attempts to simulate this idealized concept. However, real-world, actual exposure conditions are far more complex.

One complicating circumstance arises in the near field. It is readily apparent that the most intense target exposure with the resulting greatest potential for injury will occur close to the RF-radiation source. However, in this proximate region (termed the near field), the plane-wave assumptions that are true for the far field of the source's radiating antenna no longer hold. As discussed in § 3.1, the near field is characterized by complex EM field properties: the E and H fields are no longer in space quadrature (E and H vectors separated by 90°), and the value of the E/H ratio (termed the wave impedance) differs greatly from the constant value 377 Ω which characterizes the far field. In the near field, therefore, the power density concept is meaningless in its usual sense. For an object placed in the near field of an antenna the interaction is exceedingly complex because every type of antenna possesses near-field characteristics that are unique to that type of radiator. Consequently, every phenomenon involving near-field exposures must be individually analyzed and characterized. Although it is possible to predict the field distribution that exists spatially in the near field of an antenna, this distribution cannot be used as a basis for predicting the absorptive properties of an object placed in this field because the object will substantially alter that field distribution, as well as alter the radiating characteristics of the antenna itself. When an object is placed in the near field of an antenna, it will interfere with the basic purpose for which most antennas are designed, namely, the efficient transfer of RF energy from source to far field. This is because an object in the near field tends to load the antenna capacitively, thereby creating an impedance mismatch condition. As a result, some of the transmitting source's energy output is reflected by the antenna back to the source. In general, the closer the object is to the antenna, the greater is the mismatch condition, and the poorer is the transfer of radiated energy to the far field. Consequently, it is reasonable to conclude that whole-body-averaged SAR values in the near field do not greatly exceed those existing at the beginning of the far field although there may be regions within the object of high energy deposition. The limited data available from EM models involving near-field exposure (see § 3.2.3) seem to confirm this conclusion.

A secondary aspect of near-field exposures involves the unwanted exposure to leakage fields emanating from RF devices, such as microwave ovens, RF heat sealers, and diathermy units, which are not intended to radiate energy beyond their immediate surroundings. Such leakage fields are complex, and exposure invariably takes place in the near zone of the leakage source. Nevertheless, the limited data available from near-field exposures of EM models to leakage fields seem to show that whole-body-averaged SAR values are lower than might otherwise be expected because of the leakage-source and near-field interaction effects.

Another aspect of real-world exposures is the so-called multipath problem. People usually stand on the ground and are not suspended in space as in the idealized exposure concept; furthermore, they frequently stand close to buildings or to other reflective surfaces. This situation creates the multipath problem, in which a subject is exposed to scattered as well as to direct energy. Some of these effects are illustrated in Figure 3-8, which shows that there is a considerable enhancement in energy absorption occurring for various multipath conditions. These effects have been illustrated using the prolate spheroid representation of a 70-kg man. Note that when the model is in contact with a conducting ground plane, there is a doubling of the resonant whole-body energy absorption compared to that of free-space (Case II vs. Case I). Furthermore, if the model is standing at a distance (Case V) in front of the reflecting plane that corresponds to an eighth of the incident wavelength (0.125 λ), there is a tenfold increase in absorption relative to that of free space. Even greater increases are recorded when the model is placed at a critical point inside a 90° corner reflector (Cases IV and VI); however, these cases are exposure situations unlikely to occur in actual practice. In addition to these multipath effects, a further enhancement of energy absorption can occur because of proximity effects that are created when two or more subjects are simultaneously irradiated. Gandhi _et_ _al_. (1979) have found that when subjects are spaced by a critical separation of 0.65 λ, a 50-percent enhancement in absorption can occur. Coupling of RF energy into biological systems

RATE OF WHOLE-BODY ABSORPTION (WBA) IN WATTS FOR A PROLATE SPHEROID MODEL OF MAN (weight = 70 kg, height = 1.75 m) AT 10 mW/cm^2

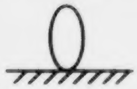
Nonresonant conditions

WBA	SAR
38 W (no reflectance)	0.54 W/kg
19 W (50% reflectance)	0.27 W/kg

Case I. At resonance for free space.

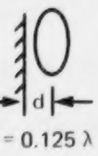
WBA	SAR
151 W	2.16 W/kg f = 62-68 MHz

Case II. At resonance for conditions of electrical contact with the ground plane.



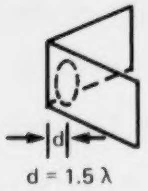
WBA	SAR
2 x 151 = 302 W	4.31 W/kg f = 31-34 MHz

Case III. At resonance for placement in front of a flat reflector.



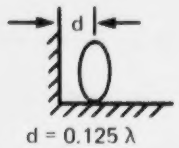
WBA	SAR
4.7 x 151 = 710 W	10.14 W/kg f = 62-68 MHz

Case IV. At resonances for placement in a 90° corner reflector.



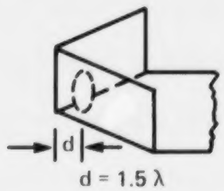
WBA	SAR
27 x 151 = 4077 W	58.24 W/kg f = 62-68 MHz

Case V. At resonance in electrical contact with ground plane, in front of a flat reflector.



WBA	SAR
2 x 710 = 1420 W	20.28 W/kg f = 31-34 MHz

Case VI. At resonance in electrical contact with ground plane in a 90° corner reflector.



WBA	SAR
2 x 4077 = 8154 W	116.48 W/kg f = 31-34 MHz

Figure 3-8. Absorption dependence on various ground and multipath factors (Gandhi et al. 1977). Note that these data are based on experimental measurements.

is discussed further in the RF Radiation Dosimetry Handbook (Durney et al. 1978, pp. 27-40).

3.2.2 RF Dosimetry Definitions

Dosimetry is the measurement or estimation of RF energy or power deposition in an irradiated subject, including the internal distribution of that deposited energy. In recent years, the terminology describing dosimetric assessment has been evolving. Prior to the mid-seventies most investigators used terminology that appears to have been conveniently borrowed from the ionizing radiation field and that employed the same cumulative dosage concept (Youmans and Ho 1975; Justesen 1975). Many investigators felt that this terminology was inappropriate for use with nonionizing or RF radiation because energy absorption in this case is not considered a cumulative phenomenon in a way that has been accepted for ionizing radiation (Susskind 1975; Guy 1975). Consequently, a new terminology was proposed that did not use the word "dose." The now widely accepted term "specific absorption rate" was first suggested by the late Curtis Johnson (1975) to replace "dose rate," the term used until then for the absorption rate per unit mass. The National Council on Radiation Protection and Measurement (NCRP 1981) has formally recommended adoption of the term SAR in RF dosimetry. NCRP has also endorsed use of the term "specific absorption" (SA) for the absorbed energy per unit mass (referred to earlier as "dose").

Table 3-2 lists the various RF dosimetric quantities in general use, together with their definitions and units. Although the terms (particularly

TABLE 3-2. PROPOSED SYSTEM OF RF DOSIMETRIC QUANTITIES, DEFINITIONS, AND UNITS*

Quantity and Definitions	SI Unit (Preferred)		Other Units Used
	Name	Symbol	
Whole-Body Absorption (formerly integral dose) The total EM energy absorbed by the irradiated subject	joule	J	millijoules (mJ) (1 mJ = 10^{-3} J) calories (1 cal = 4.187 J)
Whole-Body Absorption Rate (formerly integral dose rate) The time rate of total EM energy or total power absorption by the irradiated subject	watts	W	milliwatts (mW) (1 mW = 10^{-3} W) cal/min
Specific Absorption (formerly dose) The mass-normalized EM energy absorbed by the irradiated subject	joules per kilogram	J/kg	mJ/g cal/g
Specific Absorption Rate (formerly dose rate) The mass-normalized rate of energy or mass-normalized power absorbed by the irradiated subject	watts per kilogram	W/kg	mW/g cal/g-min
Absorption Density (also absorbed energy density or energy density, dissipated) The volume-normalized EM energy absorbed by the irradiated subject	joules per cubic meter	J/m^3	mJ/cm^3
Absorption Rate Density (also absorbed power density, density of absorbed power, heating potential, etc.) The volume-normalized rate of EM energy or volume-normalized power absorbed by the irradiated subject	watts per cubic meter	W/m^3	mW/cm^3 (1 mW/cm^3 = 10^3 W/m^3)

*Throughout this table, "absorption" refers to RF-energy absorption.

SA and SAR) for some of these quantities have now gained widespread acceptance, other terms, particularly those dealing with the volume-normalized power or energy absorption, have only recently been proposed and have not yet gained wide acceptance.

The mass-normalized and volume-normalized absorption rates are directly related through the localized or whole-body-averaged tissue mass density ρ, that is, absorption-rate density, ARD = ρ(SAR), where ρ is in kilograms per cubic meter. Most biological tissues are composed largely of water so that it is reasonable to assume a unity tissue density value. In this case, the two quantities are numerically equivalent. This approach has been adopted by many of those engaged in predictive EM modeling (see § 3.2.3, Analytical and Numerical RF-Electromagnetic Interaction Models) where the model is composed of some homogeneous tissue having average physical and dielectric characteristics that are representative of the various tissues of the body being modeled. For example, all of the SAR data given in the familiar _RF Dosimetry Handbook_ were derived this way; the assumption of a unity average tissue density is specifically stated (Durney _et al_. 1978).

It should be noted that, for both the mass-normalized and volume-normalized quantities listed in Table 3-2, there exists a subset of two additional values. These are a) the whole-body-averaged value, which represents the overall absorption or absorption rate divided by the total mass or volume of the subject, and b) the localized value, which describes the absorption or absorption rate in an incrementally small mass or volume at some given point within the subject. The localized ARD is mathematically defined by the expression σE^2, where σ is the local tissue conductivity, and E represents the root mean square value of local internal E-field strength.

So far, there has been no discussion of radiant exposure rate assessment, i.e., measurements of the incident field strength or power density. Regrettably, many workers continue to include such assessment under the general heading of "dosimetry." Such inclusion is technically incorrect, because the exposure rate is not an assessment of dose even though the two may be related. The correct terminology for incident power-density assessment is "densitometry," which should not be confused with dosimetry. Experimental methods used in densitometry are discussed in § 3.3.3, Densitometric Instrumentation. The various experimental techniques which have been developed for whole-body as well as localized or regional dosimetry are discussed in detail in § 3.4, Experimental Methods.

3.2.3 Analytical and Numerical RF-Electromagnetic Interaction Models

Much of the discussion concerning the qualitative nature of EM interaction with biological targets contained in § 3.2.1 is based on data derived from mathematical EM models in conjunction with limited experimental confirmation. Predictive physical modeling, used extensively in this research area by many workers during the past 25 years, has contributed significantly toward an improved understanding of the nature of EM field interactions with biological subjects and their absorption characteristics. In these models an object of simplified geometry, composed of dissipative dielectric materials that closely simulate the spatially averaged electrical properties of biological tissues is irradiated by some form of noncomplex incident field such as a unipath plane wave. Solutions to the problem setup in the model can then be derived using several well established analytical and numerical techniques. Actual computations are performed using high-speed digital computers, and the outputs represent whole-body-averaged and localized ARD, absorption cross sections, and absorption coefficients.

Besides the improved understanding of the EM interaction process already mentioned, modeling has proved to be important for two more basic reasons. First, mathematical modeling and experimental measurements on scaled-down doll and figurine phantoms have so far provided us with the only practical method of gaining qualitative and quantitative insight into the absorption characteristics of the human body under various conditions of irradiation. Any attempt to make absorption measurements on actual human subjects has so far proven impractical because of technical difficulties, high costs, and ethical considerations. Reasonably accurate quantitative data on human-absorption characteristics are necessary to determine the objective exposure limits for RF radiation. The reasons are discussed below.

The 1974 ANSI-recommended protection guide (ANSI 1974) is based on an allowable exogenous heat load due to RF-energy absorption and conversion that cannot exceed the basic metabolic rate (BMR) in an adult man (~ 70 to 100 W). For a 50th percentile standard-size man weighing 70 kg, this corresponds to a whole-body-averaged SAR of ~ 1 to 1.4 W/kg. To determine the power density level of incident radiation that will create this exogenous heat load in man, a detailed knowledge of human RF-absorption characteristics is required. At the time that the first RF-radiation protection guide was proposed in the early fifties, virtually no data existed on the RF-absorption characteristics of humans, and, consequently, the assumption had to be made that the EM absorption cross section for humans was equivalent to man's geometric cross section, which is ~ 1 m^2 (i.e., a unity absorption coefficient was assumed). From this came the well known exposure limit of 10 mW/cm^2. During the past 10 years or so, a considerable accumulation of data based largely on human interaction modeling has been developed (discussed later in this section). These data showed that under resonant conditions, the RF-absorption cross section of humans can be 4 to 8 times greater than the geometric cross section. Thus, at resonance, the RF-absorption rate for humans can potentially exceed the BMR by this factor when exposure is to incident radiation levels of 10 mW/cm^2. Such a situation clearly constitutes an excessive thermal burden for exposures of indefinite duration. Thus, EM modeling has played a significant role in demonstrating that, under certain conditions, the originally recommended exposure limit is potentially unsafe, and in providing an objective basis for the revision of that guideline.

The second reason for the importance of EM modeling is that it provides us with a method of extrapolating absorption data from animal experiments for application to humans. Using the prolate spheroid representation for humans and animals, a considerable amount of data has been compiled on whole-body-averaged SAR vs. frequency characteristics for several different species. These data are given in the Radiation Dosimetry Handbook (Durney et al. 1978); highlights of this material are presented in Table 3-3, which shows the resonant frequency range (long axis oriented parallel to E field) and the whole-body-averaged SAR at resonance, normalized to an incident field level of 1 mW/cm^2 for five different species, including humans. The data given in Table 3-3 enable a researcher to readily determine for a particular animal species the resonance frequency range to be used during experimentation. For example, to simulate human resonance in adult rats, exposure would have to be at a frequency in the range of 600 to 700 MHz. This is an example of "frequency scaling", or adjusting the frequency at which an experimental animal is exposed in order to approximate certain given conditions of human exposure. In

TABLE 3-3. RANGE OF RESONANT FREQUENCIES OF MAN AND ANIMALS IRRADIATED BY PLANE WAVES IN FREE SPACE AT 1 mW/cm^2 WITH LONG AXIS PARALLEL TO THE ELECTRIC FIELD*

Species	Average Weight (kg)	Average Length (m)	Resonant Frequency (MHz)	RMR (W/kg)	Average SAR (W/kg)
Man (av)	70	1.75	70-80	1.26	0.25
Woman (av)	61	1.61	80-90	1.15	0.25
Child (10 years old)	32.2	1.38	90-100	2.00	0.35
Rhesus monkey (seated)	3.5	0.04	300-350	2.36	0.30
Dog (beagle)	13.5	0.06	200-250	1.72	0.16
Guinea pig	0.58	0.02	550-600	3.83	0.55
Rat (medium)	0.32	0.02	600-700	4.8	0.75
Mouse	0.02	0.007	2400-2600	6.5	0.72

*Data derived from Durney et al. 1978.

addition, differences in the whole-body-averaged SAR between the two species must be considered; from the last column of Table 3-3, it is evident that, at resonance, the whole-body SAR for the rat is 3 times that of a human. Thus, if a certain SAR value is obtained in a rat when exposed at a 10-mW/cm^2 level, roughly 3 times that level, or 30 mW/cm^2, is needed to obtain the same SAR value in humans (resonant condition for both).

The data shown in Table 3-3 can likewise be used to determine whether a given exposure frequency falls in, above, or below the resonance range for humans. As was discussed earlier, these three categories lead to fundamental differences in absorption as well as patterns of internal energy deposition. There will likely be a corresponding difference in biological effects seen in the different frequency ranges, with the resonant range representing the potentially most hazardous condition because of the high absorption efficiency and highly nonuniform internal deposition of energy. As already emphasized, proper simulation of a given human exposure scenario using experimental animals requires the use of 1) frequency scaling to ensure that the type of interaction taking place is roughly comparable (i.e., subresonant, resonant, or supraresonant), and 2) appropriate adjustment of the incident exposure level to obtain a specified whole-body-averaged SAR or, where possible, a given localized SAR in some specified target organ. To check for the possibility of any effects that might be specific to a particular frequency to which humans are being exposed, animals must necessarily be exposed to that same frequency. Given such an experiment, the use of frequency scaling is obviously inappropriate.

3.2.3.1 Model Details--

Gandhi (1980) and Durney (1980) published excellent reviews on EM modeling, summarizing most of the major research contributions to 1980 and detailing the status of the EM modeling field at that time. Consequently, the material that follows will not duplicate these reviews, but will instead trace the historical development of EM models with emphasis on the increasing complexity of such models and their application. Only a few relevant publications in the field will be cited; the interested reader is referred to Gandhi's and Durney's reviews for more complete details as well as to the RF Radiation Dosimetry Handbook (Durney et al. 1978, pp. 64-71), which contains a comprehensive literature survey of all theoretical and experimental modeling work performed to 1977. The interested reader is also referred to the original publications for further details of the mathematical techniques used to solve the various problems that are discussed below.

Planar and spherical models--The earliest model considered involved the one-dimensional solution to the planar tissue slab irradiated by a plane wave (Tell 1972). The slab is infinitely wide and can contain several layers of different tissues. Although the solution to this problem is straightforward, the model is restricted in its application because it does not account for the obvious closed-form shape of all human and infrahuman bodies. The only situation for which this particular model is valid is the case where the wavelength is small compared to the system size, as depicted earlier in Figure 3-6, case C; for human irradiation, such wavelengths correspond to frequencies above approximately 3 GHz. The concept of "penetration depth" originated from this one-dimensional model. The penetration depth is the depth within the tissue slab where the RF energy has been attenuated to a value of 1/e, or 36.8 percent of its value at the planar surface. Strictly speaking, this concept applies only to this particular planar model. It is unfortunate that the concept has been extensively borrowed and frequently is inappropriately used in discussions of RF absorption in nonplanar models where the wavelength is either longer than or comparable to the object size. It must be emphasized that the penetration depth concept can be accurately applied only when the wavelength is small compared to the object size.

The next level of complexity involves two-dimensional solutions of the infinitely long cylinder with circular, elliptical, and arbitrary cross sections; some of these models are of homogeneous tissue and others are multilayered (Ho 1975). These models are primarily intended to simulate RF heating in human limbs under conditions of plane-wave irradiation and using a rectangular applicator in contact with the cylindrical model; the latter problem is of particular interest to diathermy practitioners. Ruppin (1979) examined a lossy-dielectric cylinder model placed in front of a perfectly conducting plane (i.e., a multipath problem). His data show both enhancement and reduction of average SAR relative to the isolated cylinder, depending on the conditions of irradiation.

The first attempts at three-dimensional solutions involved homogeneous spheres of tissue-equivalent dielectrics. Although only a poor approximation to the actual shape and heterogeneous dielectric composition of humans and experimental animals, the sphere model has been used extensively because of the ready availability of solutions based on the classical Mei theory involving spherical wave functions (Stratton 1941). These methods can be readily programmed on high-speed machines that yield data on the EM absorption cross section and on the distribution of localized ARD for homogeneous spheres (Kritikos and Schwan 1975). (Some approximations made by Kritikos and Schwan [1975] can be used in the subresonance or Raleigh region and the supraresonance or quasi-optical region, greatly simplifying these computations.) This work demonstrated that a highly nonuniform absorption distribution is obtained under resonant conditions, including the formation of relatively intense "EM hot spots" near the sphere's center (Figure 3-9). Other workers (Weil 1975) have used a multilayered spherical model that consists of several concentric layers of different tissues representing an idealized model of an adult, child, or monkey head exposed to plane-wave radiation. However, this concept has obvious limitations because the spherical model is spatially isolated, whereas, in reality, the head is attached by the neck to the body's trunk. Results for the multilayered sphere were similar to those obtained for the homogeneous sphere with the exception that, in the supraresonance region, enhanced absorption was noted in the multilayered model. This enhancement is caused by the presence of the surrounding layers of skin and fat, which appear to provide an impedance transformation mechanism by which energy transfer into the sphere is increased. A recent paper by Barber *et al*. (1979) has shown that a planar model can accurately predict this enhancement effect for any three-dimensional nonplanar shape, and that the layering enhancement factor can be applied to any nonlayered object, such as a human model, to predict the absorption characteristics of the layered object.

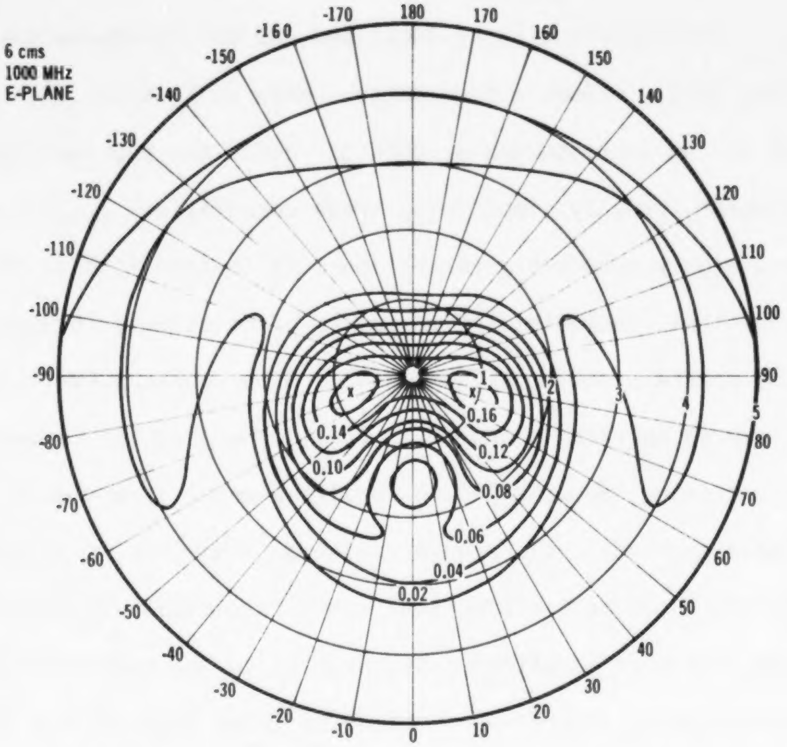


Figure 3-9. ARD distribution in core of 6-cm radius multilayered sphere at 1650 MHz (Weil 1975).

The effects of altering irradiation from plane wave to near field on the absorption characteristics of multilayered sphere models were investigated by Hizal and Baykal (1978). They found that EM hot spots continue to occur when the model is excited near resonance in the near field of a loop antenna, but not when similarly excited by a dipole antenna.

Prolate spheroidal and ellipsoidal models--Since prolate spheroids and ellipsoids are much better approximations to actual human and animal shapes, using these models was a logical next step to solving this problem. While in principle it is possible to obtain solutions to the prolate spheroid and ellipsoid problem in spheroidal and ellipsoidal wave functions in the manner already accomplished for the sphere, in practice this has not been possible because of many mathematical difficulties. Consequently, workers have resorted to using several different approximation techniques, further details of which may be found in Durney's review (1980). Such methods have provided accurate data on absorption in the subresonant and near-resonant region, as well as in the supraresonant or quasi-optical region. These data have been compiled in the RF Dosimetry Handbook (Durney *et al*. 1978, pp. 75-106) in whole-body-averaged SAR vs. frequency plots for many different animal species. However, under some conditions, there is a gap covering the resonant and immediate post-resonant regions, where these approximations no longer hold. Using approximate data derived from antenna theory and experimental observations, it has been possible to bridge this gap with the aid of curve-fitting techniques. This is illustrated in Figure 3-10, which shows SAR data for a prolate spheroidal model of man for the three basic orientations of the model's long axis relative to the E, H, and k vectors. Note the strong orientation effect discussed earlier. Durney *et al*. (1978, 1979) have also developed a useful empirical formulation that describes the E-field polarization curve shown in Figure 3-10. It can be programmed on a hand calculator and yields reasonably accurate SAR data for a prolate spheriodal model of any size of eccentricity.

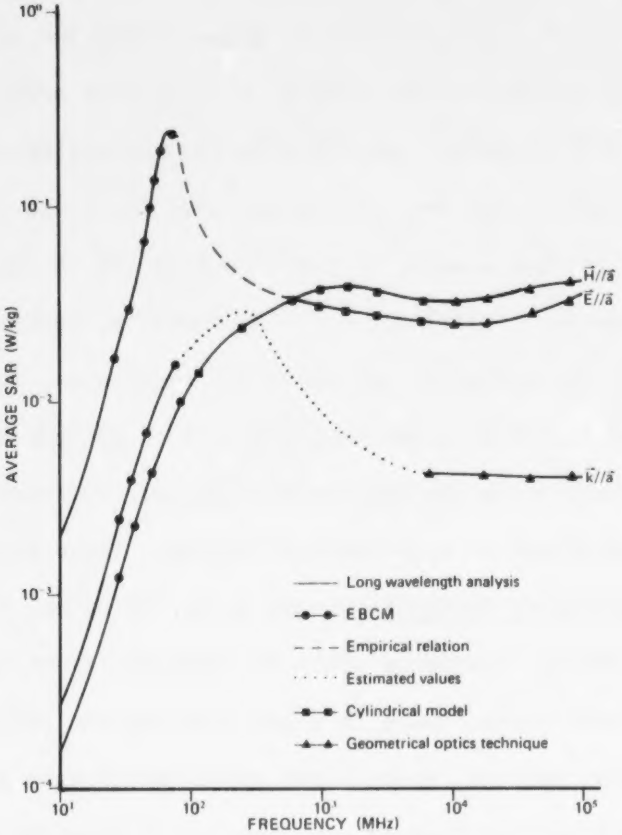


Figure 3-10. Curve fitting of SAR data for a prolate spheroidal model of man for the three basic orientations of the model's long axis relative to the E, H, and k vectors of an incident plane wave (1 mW/cm^2 power density). Taken from Durney et al. (1978).

As discussed earlier, an isolated model, regardless of shape, that is suspended in space is an inappropriate representation of the real-life conditions under which humans are exposed. A prolate spheroidal model in contact with or in close proximity to a conductive ground plane is an obvious improvement over the isolated model. Iskander et al. (1979) have analyzed such a model by both antenna and circuit theory. In this model, the finite separation between feet and ground created by the usual presence of footwear can be accounted for by introducing a lossy capacitor in the equivalent electrical circuit of the prolate spheroid. From Iskander's data (Figure 3-11), it is apparent that the primary effect of the ground plane is to shift the SAR curve for the isolated model to the left with only a slight evident increase in peak SAR. This means that the resonant frequency of the prolate spheroidal model of man is shifted from ~ 75 MHz to 45 MHz when the model is in perfect contact with a conducting ground plane; the intermediate case shown, in which resonance occurs at 55 MHz, represents imperfect contact between model and ground plane due to a 3-cm lossy gap. The latter case is probably the most realistic of the three considered. Iskander _et_ _al_. also concluded that when the model is separated from the ground plane by a gap of 7.5 cm or more, the whole-body SAR values are essentially the same as those for the isolated model.

It is evident from oral presentations at recent (1978-1980) scientific meetings that much effort is being devoted to analyses of the absorption of prolate spheroid and other models in the near field of an antenna. Iskander _et_ _al_. (1980) have studied such a problem for a prolate spheroid model of man in the near field of a short electric dipole at 27 MHz. They found that average SAR values in the near field tend to oscillate about the constant value predicted for plane-wave irradiation. There are also significant alterations in the internal distribution of deposited energy in the near field.

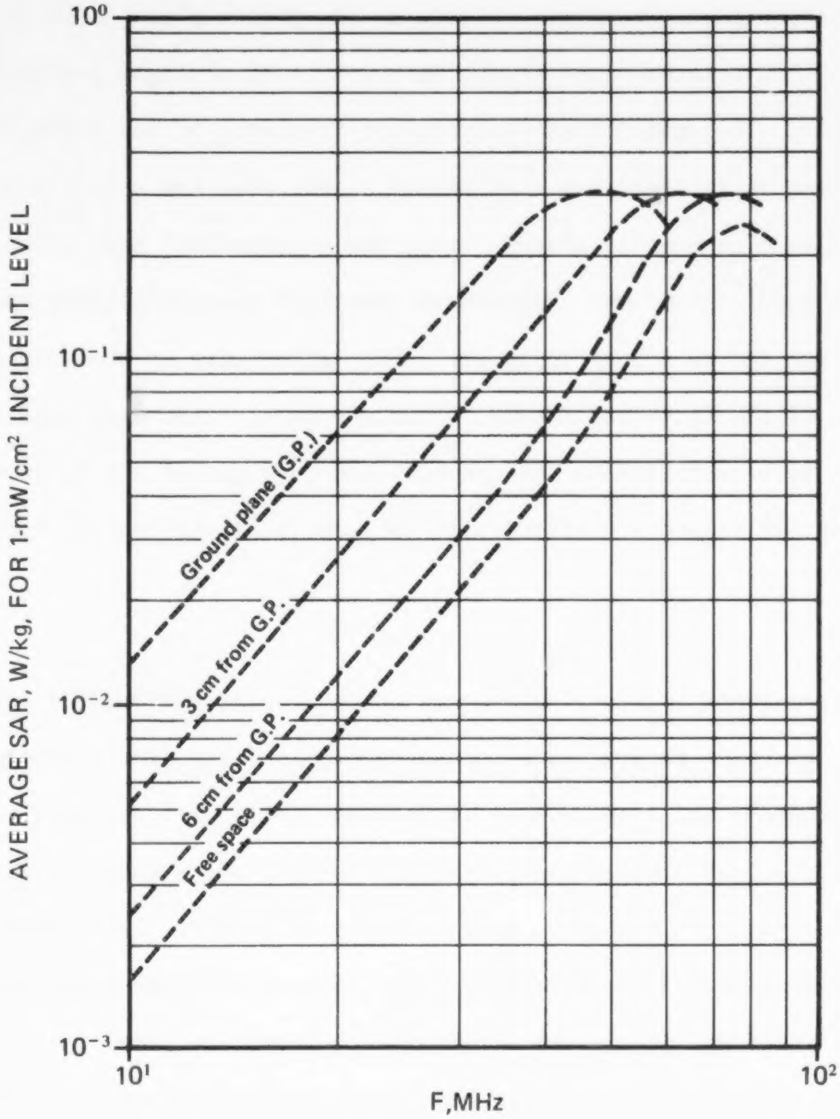


Figure 3-11. Effect of a capacitive gap on average SAR between the man model and the ground plane (Iskander et al. 1979).

As discussed previously, the data developed on prolate spheroidal and ellipsoidal models have played an important role in extrapolating RF absorption data from lower animals to man. Nonetheless, it should be emphasized that these data have limitations: the solutions are not exact but are approximations, yielding data that are accurate enough (± 10 percent) for most practical applications. Furthermore, with the exception of the subresonant region (long wavelength analysis, Figure 3-10), existing solutions provide data on only the whole-body absorption characteristics of this model. No data are yet available on the three-dimensional ARD distribution and EM "hot spot" formation potential in the resonant and immediate supraresonant region. Such data would be of potential value to those engaged in experimentation with rodents because of the close similarity between the rodent shape and the prolate spheroid shape.

Human block models--Although prolate spheroidal and ellipsoidal models are reasonably accurate representations of many laboratory animals, particularly rodents, this is not true of the primates, including man, because the appendages (head, arms, and legs) are much larger and more significant. The importance of these appendages is underscored by experimentation using saline-filled dolls and scaled-down human phantoms (Guy et al. 1977), which showed relatively intense localized absorption in the ankles, legs, and neck. Since it was impossible to confirm the localized effects with the prolate spheroidal model, attempts were made to develop a more realistic human model in which numerous cubical cells form a so-called block model of man (Figure 3-12). The EM solution to this type of sophisticated problem is realized through the solution of a large system of simultaneous equations using matrix inversion or

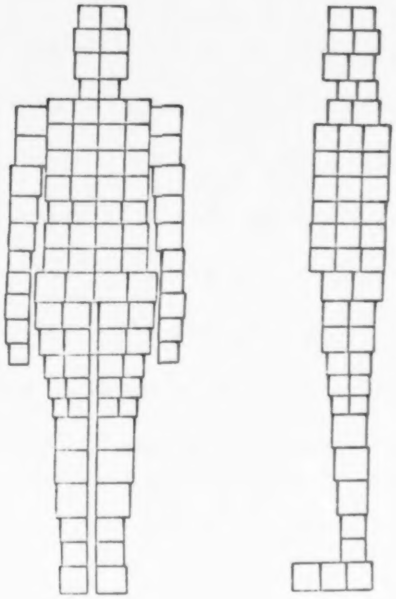


Figure 3-12. A realistic block model of man (Hagmann *et al*. 1979a).

iterative techniques. Further mathematical details are given in Durney's review (1980). Such solutions can be obtained only by using dedicated large-scale computing facilities with expensive memory capability. Furthermore, because of finite lijits in the average memory capacity of all but the largest computers available, there is a limit to the number of cubical cells that can be used to make up the model. The accuracy and resolution of the solutions are dependent on cell size. In the work of Chen and Guru (1977), a maximum of 108 cells was used, whereas Hagmann *et al*. (1979a) used 180 cells. These limits inevitably reduce the spatial resolution with which the localized absorption distribution can be determined in the model, and they place an upper limit on the frequency range over which solutions are valid. (Note that this range does include the resonant and immediate supraresonant region.) Since this technique readily allows for differences in the dielectric properties of individual cells in the models, it is possible to approximate the inhomogeneous tissue properties of the human body, but there is a limit to how finely such inhomogeneities can be modeled.

Figure 3-13 shows some data obtained for the human block model (Figure 3-12) when it stands on a ground plane and is irradiated by a vertically polarized plane wave. The curve labeled "whole body" gives the whole-body-averaged SAR throughout the model, which agrees closely with that obtained for the equivalent prolate spheroidal model in contact with a ground plane; whole-body resonance also occurs at ~ 45 MHz. Two significant conclusions may be drawn from these data: (a) At whole-body resonance, the localized SAR in the legs is about five times that of the whole-body average, indicating the potential for relatively intense absorption in the legs; and (b) part-body resonances exist for the arms and for the head at frequencies of ~ 150 and 375 MHz, respectively. Localized SAR values for the neck are seen to be relatively high throughout the frequency range 100 to 400 MHz. The significance of the head-resonance effect has been emphasized by Hagmann _et_ _al_. (1979b), who modeled the head and neck with much improved resolution. In this study, the detailed head is attached to the same torso model used earlier (Figure 3-12), so that the head is not isolated as in previous studies involving inhomogeneous spherical models (Weil 1975) and block models of isolated human and infrahuman heads (Rukspollmuang and Chen 1979). The Hagmann _et_ _al_. data show

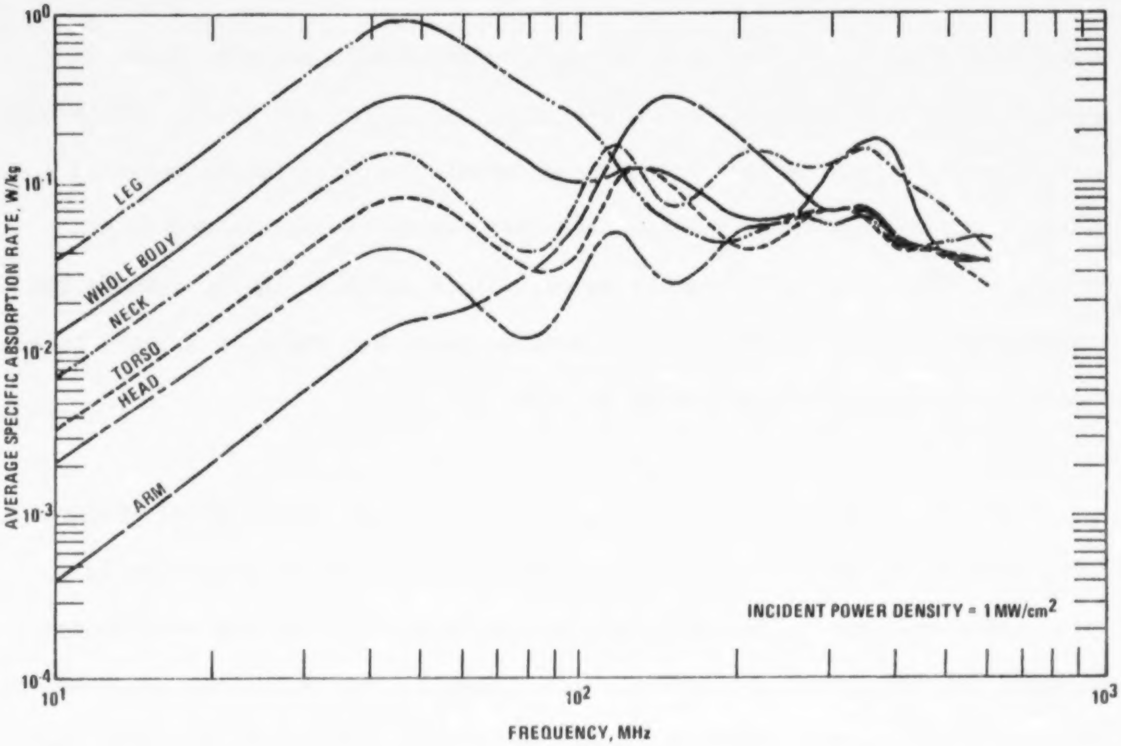


Figure 3-13. Absorption for man block model standing on ground plane (Gandhi et al. 1979).

strong localized absorption at the front and back of the neck and in the center-base region of the skull; localized SAR values are two to four times the whole-body average.

RF absorption in block models when irradiated under near-field conditions is being studied by some workers. Chatterjee et al. (1980) reported a study involving the near-field interaction of the human block model (Figure 3-12) with the measured leakage-field distribution of an industrial RF heat sealer operating at 27 MHz. Their data show that averaged and localized SAR values are much lower for near-field exposure than is the case for plane-wave exposure at equivalent power density levels.

3.2.3.2 Accuracy--

As discussed already, this document and the 1982 ANSI guideline (ANSI 1982) recommend frequency-dependent exposure limits that have been derived mostly from the EM modeling data just described. The validity of this approach, therefore, depends strongly on the accuracy of these data. One may conclude that the accuracy of the whole-body-averaged absorption data is good (certainly within ± 10 percent). The good agreement obtained between data for the human prolate spheroidal and block models appears to support this contention. However, the accuracy of the localized absorption data is probably inferior. This is particularly true of the block models where accuracy is probably no better than ± 50 percent, owing to the limitations on numbers of blocks available. On the other hand, localized absorption data for the spherical model as well as those available for the prolate spheroid are more accurate, since they were derived using more rigorous techniques.

3.2.3.3 Unresolved Questions--

The need for additional modeling has been discussed by Durney (1980). Improvements and refinements in existing block models are needed, especially in spatial resolution and accuracy; the same is also true in modeling tissue inhomogeneities. In coming years, a new generation of "superpower" computers with greatly enhanced computational speeds--an order of magnitude increase over existing machines--will undoubtedly become available for scientific studies. Such computers will almost certainly be used to refine existing EM absorption models, particularly in spatial resolution problems and in solving more complex problems that hitherto have not been attempted because of computer limitations.

As Durney (1980) emphasized, there is still a need for more solutions to near-field interaction problems, since the near field more frequently represents the real-life situation to which people are exposed. Though models involving near-field irradiation are considerably more complex to solve than are those for the far field (plane wave), it should be possible to attempt the solutions of these based on our existing knowledge of plane-wave solutions.

3.2.4 Mechanisms of RF Interaction with Biological Systems

Biophysical models that relate molecular structure to the interaction of RF radiation with biological systems provide a base for understanding the potential hazards of this type of RF radiation and for designing relevant experiments. The purpose of this section is to review these interactions and, where possible, to discuss the changes in structure and biological function that may result.

3.2.4.1 Complex Relative Permittivity--

The molecular-level interactions may be averaged over a macroscopic biological sample and characterized by an average interaction parameter called the complex relative permittivity (ε^*) of the sample. This interaction parameter facilitates discussion of the effects of a biological sample on thermodynamic properties. It is a measure of the capacity of the charge distribution within the sample to adjust to a change in an applied electric field. This measure is composed of two parts, the real component of the complex permittivity (ε') and the imaginary component of the complex permittivity (ε''). The real component is a measure of the energy stored in the charge distribution of the sample by the interaction with the field. The imaginary component is related to the energy dissipated by the field in the sample. Initially, the dissipated energy may be restricted to just a few molecular modes within the sample. Eventually, the dissipated energy will be thermalized, but temperature gradients may persist within the sample if the rate of energy dissipation is a function of position, due to the geometry of the sample or to field gradients or differences in ε'' within the system. Finally, after the RF-radiation exposure has ceased, the dissipated energy will be equally distributed throughout the sample and will result in either a change in sample temperature or a transfer of thermal energy from the sample as well as possible chemical and structural changes.

The ε^* of many biological tissues has been measured by several investigators. Some excellent reviews are available (Schwan 1957; Johnson and Guy 1972; Durney _et al_. 1978; Stuchly and Stuchly 1980; and Schwan and Foster 1980). Complex relative permittivity is a function of frequency over our region of interest.

Table 3-4 shows the values of ε' and ε'' (abstracted from Durney _et al_. 1978; Schwan and Foster 1980; Stuchly and Stuchly 1980). The dielectric properties of muscle tissue have been used to characterize the dielectric properties of all biological tissues with a high water content (Schwan 1957;

TABLE 3-4. DIELECTRIC PERMITTIVITIES FOR VARIOUS TISSUES*

Tissue Type	Dielectric Value	Frequency (MHz)							
		0.1	1	10	50	100	10^3	10^4	1.7×10^4
Muscle	ε'	3×10^4	2×10^3	220	90	75	54	40	34
	ε"	10^5	10^4	1.2×10^3	400	80	27	21	21
Brain	ε'			240	110	80	40	35	
	ε"		2.6×10^3	500	180	95	16.5	15	
Liver	ε'	10^4	1.5×10^3	240	90	78	46	36	
	ε"	5×10^4	5×10^3	800	195	110	18	11	
Bone	ε'	8.0			7.2		5.8	4.9	
	ε"	0.5			10.8		1.3	0.7	
Fat	ε'				12	10	6.0	4.0	
	ε"				17	12	2.0	0.7	

*These values are abstracted from reviews by Schwan and Foster (1980) and Stuchly and Stuchly (1980). The original sources are quoted therein. The values have been chosen in the middle of the range for experimental values. Reported values may differ from one another by as much as a factor of two.

Schwan and Foster 1980). This characterization also serves as an illustration of some of the underlying phenomena responsible for ε*. Figure 3-14 shows the ε' of muscle as a function of frequency.

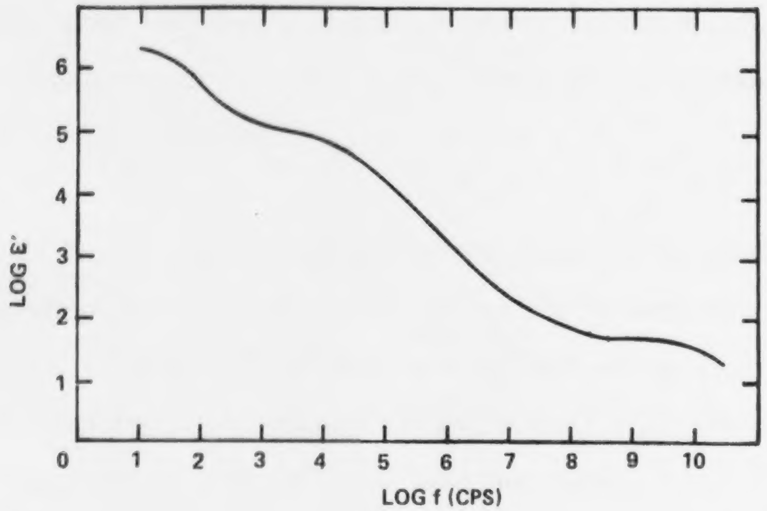


Figure 3-14. The real component of the complex permittivity of muscle (ε') as a function of frequency (f) from the values for muscle (Schwan 1957).

It can be seen in Table 3-4 that in the region between 0.5 MHz (the lower end of the range of interest) and ~ 50 MHz, the complex permittivity of muscle decreases by two orders of magnitude. However, between 100 MHz and 10 GHz it decreases by < 50 percent; and again, at frequencies above ~ 10 GHz, but still within the range of interest, the real component of complex permittivity decreases rapidly.

The imaginary component of the complex permittivity (ε") has two components--one due to the movement of free charges, and the other to the orientation of either permanent dipoles or dipoles resulting from the interaction of the field with polarizable microscopic structures. The former component will be proportional to the inverse of the applied RF-radiation frequency; energy absorbed this way acts directly to heat the sample. The modes of absorption of the latter component relate to the specific structure of biological molecules and molecular complexes, and this component has a maximum where the real component of the complex permittivity ε' is changing most rapidly.

Frequency regions with rapidly changing dielectric parameters indicate that a particular component of the system, or a particular type of response to the field, is reaching the limit of its capacity to respond (i.e., at higher frequencies the field is changing too rapidly for a particular component to respond). It has been suggested that the rapid change in the region below 50 MHz results from polarization effects in which cellular membranes are charged by the surrounding electrolytes (Schwan and Foster 1980). Another response that is limited to this low frequency range is the rotation of large dipolar macromolecules or molecular complexes orienting with the changing field (Takashima and Minikata 1975). The dielectric response below 50 MHz may result from more than one mechanism. The response above ~ 5 GHz results from the rotation of water molecules in the biological systems, and it is similar to the response seen in pure water. It has been postulated that a small decrease in ε' observed near 1 GHz results from rotations of water molecules constrained by their interaction with large molecules and molecular complexes (Schwan 1965; Grant _et_ _al_. 1968) and, therefore, these water molecules are not able to respond to the field at higher frequencies.

The general features of ε^* of biological tissues can be explained in terms of the major molecular and structural components of the tissues. However, biological systems are inhomogeneous and inherently complex at the molecular level, and interaction with a minor molecular component may have negligible influence on the dielectric parameters of tissue (an average property of a macroscopic volume) but may interfere with the capacity of that minor component to perform its biological function.

Therefore, it is useful to discuss the specific mechanisms for the absorption of RF radiation at the molecular level. Furthermore, since the mechanisms are similar for the major components, this discussion will also provide a more detailed explanation of the interactions responsible for the complex relative permittivity ε^*.

3.2.4.2 Mechanisms for RF-Radiation Absorption at the Molecular Level--

Table 3-5 presents information on the energy of an RF beam relevant to molecular level interactions. It should be noted that the binding energy of a single electron in a molecule is typically on the order of tens of electron volts, whereas excitations of electrons within molecules are on the order of electron volts, and the energy of a hydrogen bond is > 0.1 eV. Accordingly, direct linear mechanisms for the absorption of a photon or a few photons by biological molecules from an RF field cannot involve changes in electronic or covalent molecular structure, nor can they involve the breaking of hydrogen bonds. This does not imply that single photons cannot cause changes in the structure of biological molecules or molecular complexes. They contain sufficient energy to change the three-dimensional structure of biological

TABLE 3-5. ENERGY UNITS FOR RF RADIATION

λ (m)	f (MHz)	Energy/photon (eV)
10^{-2}	3×10^{4}	1.2×10^{-4}
1.24×10^{-1}	2.45×10^{3}	1×10^{-5}
3×10^{-1}	10^{3}	4.1×10^{-6}
10	3×10^{1}	1.2×10^{-7}
3×10^{2}	1	4.1×10^{-9}

molecules in a manner that leaves the covalent and hydrogen-bonded structure intact. The following paragraphs describe some of the excitations of biological molecules that can be induced by an RF field and the changes in three-dimensional molecular structure that may result.

A change in the rotational energy of dipolar molecules or molecular segments is a ubiquitous mode for energy absorption from an RF field by molecules in a biological system. The absorbing molecular structure increases its angular momentum by quantized units. The size of these units and the characteristic frequencies for absorption depend on the distribution of mass within that structure. In general, the more massive the rotating structure, the lower the characteristic frequencies.

The rotational mode of interaction is relevant through the entire range of the frequencies of interest for the purpose of this document. Free rotation of proteins and other biopolymers are modes for absorption in the frequency range from 10 kHz to 100 MHz and beyond. In addition, smaller molecules and molecular segments absorb at higher frequencies by this mode. The absorption of energy into free rotational modes does not lead to structural changes in the absorbing molecule or segment because it rotates rigidly. Through collisions with other molecules in the biological system, this initial increase in rotational kinetic energy will be dispersed throughout the various molecular motions of the system (i.e., the energy will be thermalized). With this mode of absorption, functional changes, if any, will result only from these local increases in temperature. In a biological system at normal body temperatures, an individual molecular species will absorb over a broad frequency range by this mode because of its concurrent interaction with other molecules.

Since water, which has a characteristic frequency for free rotation near 20 GHz, is the major component of biological systems, a change in the rotational energy of water molecules is the principle mechanism for absorption of microwave radiation at frequencies > 2 GHz. (The frequency range for which this interaction is likely to be important is broadened by the interaction of absorbing molecules with surrounding molecules.) At the lowest frequencies of interest, changes in molecular rotational motion may also make a significant contribution to the overall dielectric properties through the interaction of microwaves with large molecules.

For many biological molecules, segments as large as many amino acids or as small as a methyl group have some rotational freedom, but are constrained both by covalent bond(s) to the main structure of the molecule and by electrostatic interactions with other nearby molecules. This rotational freedom provides a mode for the absorption of energy from an RF field. Although this mechanism is similar to the preceding one, it has been suggested (Illinger 1970; Rabinowitz 1973) that it can result in changing the equilibrium position of the rotating segment relative to the main structure of the molecule and surrounding molecules. This structural change will most likely be reversible but could have consequences for biomolecular function. The importance of this mechanism for a biological effect of RF radiation has not been substantiated experimentally.

More complicated intramolecular motional modes involve rotation and vibration, bond stretching, and twisting. These modes will also absorb energy from an RF field and will have potentially similar effects on molecular structure and function. In general, these more complicated modes are at frequencies above the range of interest, but there is some suggestion that they are important near 10 GHz. Prohofsky *et al*. (1979) have calculated the stretching modes for an artificial double-stranded DNA polymer containing one strand of adenine that is hydrogen bonded to a strand containing only thymine. They suggest that absorption of energy into these modes may affect DNA helix melting and replication. The characteristic frequencies of these calculated modes are, however, > 40 GHz.

The amount of energy required to excite either rotational or the more complex motional modes is small with respect to the amount of energy exchanged in molecular collision at biological temperatures. This implies that, unless there are special circumstances (Illinger 1970; Rabinowitz 1973; Prokofsky et al. 1979; Ginzburg 1968), the molecular configuration that results from the absorption of energy from the RF field is not unusual. However, the relative distribution of normally occurring configurations may be affected by the absorption of energy. The effect produced may be only a relative change in a normally occurring process, and may be reversible on the molecular level. Reversibility for the molecular-level absorber, however, does not imply that the resulting--if any--macroscopic biological effect is reversible. If the unusual distribution of states does not return to the normal distribution as quickly as one would expect from strictly thermal considerations, then these effects will be much more important (Fermi et al. 1965).

Another general mechanism for the interaction of RF radiation with biological molecules results from the field-induced migration of ions associated with biopolymers. The migration may be of positively charged ions--like protons or other cations--from one negatively charged site to another within the same biopolymer (Kirkwood and Schumaker 1952) or from the polarization of the ionic cloud that surrounds the biopolymers (Schwarz 1972). The distinction between these two mechanisms has been made because in the case of the former, the migration of the ion(s) may directly affect the function of the biopolymer if the migrating ion(s) or one of the sites is directly involved in molecular function. In both cases, there will be effects on the long-range interaction between biopolymers. The minimum field strength needed for the first case can be roughly estimated from the size and shape of biopolymers, and even for rod-like structures, a field of at least 10^5 V/m would be needed. For the second case, the field strength necessary is smaller and depends on the size of the surrounding ionic cloud. The frequencies where these processes are important depends on the size and shape of the molecule (Pollak 1965). For sonically fragmented DNA segments that have a rod-like structure, broad absorption regions have been found near 10 kHz and 10 MHz (Takashima 1963; Pollak 1965).

A mechanism has been described for the direct influence of an RF-electric field on the configuration of biopolymers (Schwarz 1967). If the interaction of the field with one configuration of a biomolecular system is much greater than the interaction with other configurations, then--in the presence of that field--a shift in the relative populations of the various configurations will result. The difference in interaction energy may be due to differences in the dipole moments or in the polarizabilities between configurations. This mechanism has been demonstrated in the model protein poly(γ-benzyl-L-glutamate), or PBLG (Schwarz and Seelig 1968). In its random-coil conformation, PBLG has essentially no dipole moment, whereas in its helical conformation it has a large dipole moment ($\sim 10^3$ Debye). The presence of a field of sufficient strength can induce a transition from the coil to the helical conformation. In PBLG this mechanism is responsible for absorption of energy near 1 MHz; for the distribution of conformations to be affected significantly, the field must be greater than 10^5 V/m. (If there were systems where the change in dipole moment was larger, then the field needed would be proportionally smaller.) This change in conformation is not unusual (although the relative amounts of the two conformations are altered) or irreversible, but, as previously stated, reversibility on the molecular level does not necessarily imply that any resulting, macroscopic, biological effect is reversible. For instance, the conformations may have differing biological activities, and the products of these activities may remain even after the distribution of the conformations has returned to equilibrium.

3.2.4.3 Unresolved Questions--

The mechanisms for the absorption of energy from an RF field previously discussed have been demonstrated in solutions of biological molecules, and the response of macroscopic biological systems to these fields is consistent with these molecular mechanisms. The question that remains is: Are any of these mechanisms likely to impose a potential hazard to human health? Certainly, if enough RF energy is absorbed and converted to thermal energy, corresponding biological effects ensue. Other mechanisms have been proposed for effects at the molecular level. They require changes in molecular structure and function as the result of absorption. It is extremely likely that some changes in biomolecular structure result when RF energy is absorbed. But are these changes functionally significant? Some mechanisms for biological effects in these circumstances have been proposed. They are plausible but often not quantitative, and have not been demonstrated in biological experiments. Further research to quantitate and consider these mechanisms experimentally is needed. Since exposure to RF radiation will often lead to increased temperature, careful studies are needed to separate effects that are not due to heating from other concomitant changes in temperature.

There are two other general mechanisms at the supramolecular level that need further discussion. A theoretical mechanism has been proposed for coherent action over long distances in biological macromolecular systems that are far from thermal equilibrium (Fröhlich 1968). This mechanism has been developed to explain the extraordinarily high catalytic power of enzymes; one of its consequences is an extremely long-range interaction between macromolecules. The requirements of this model are that the macromolecules possess a metastable excited state that has a large dipole moment (> 10^3 Debye) and that its polar modes couple with elastic modes. This highly dipolar metastable state will be stabilized by the migration of ions and by the structure of the water near the macromolecular surface. One of the implications of this model for enzyme action is that interaction with an EM field that is capable of supplying energy above a critical rate will result in all of the energy going into a single homogeneous electric vibration of this system (Fröhlich 1975). This means that all the other modes of the system will be at or near thermal equilibrium, while that single mode will be far removed. Although it is unlikely that this redistribution of energy will increase the rate at which the energy is absorbed by the system, the biological consequences of putting all the energy into a single mode that is related to the functional properties of the system could be extraordinary. If that single mode relates to enzyme function or recognition, it could greatly increase enzyme function until saturation is reached. The possibility also exists of re-emission of large amounts of energy and action at sites remote from the initial absorber. The specific biological consequences of this model relative to RF-field effects on biological systems cannot be well understood until detailed characteristics of particular biological systems are included. Some data can be explained by this model (Grundler _et_ _al_. 1977); the resultant _in_ _vivo_ vibrational spectral properties of biological systems also have been discussed (Illinger 1982).

One of the interesting and relevant consequences of Fröhlich's (1968) model is that the particular biological result of RF-field interaction with a biological system may be frequency dependent. It has been suggested that the range of frequencies where this process is most likely to be significant is probably > 30 GHz (Fröhlich 1968, 1975). The actual range of applicability is uncertain, and it also may be important at lower frequencies.

Fröhlich's mechanism is general. Its applicability in real or model biological systems has not been demonstrated. For potential biological effects from RF fields, it is a possible mechanism for grouping individual photons or phonons with energies << kT (the average thermal energy). This process results in the application of energy in a significant amount (> kT) at a single locus. Effects resulting from this process could not be duplicated by adding the same amount of energy to the system by a different process.

Another set of mechanisms at the supramolecular level has been proposed recently. These mechanisms are theoretical means for the direct interaction of RF fields with microscopic biological processes that depend on naturally occurring electric potentials. In general, these mechanisms depend on a nonlinear response to an applied field by the cell membrane.

Barnes and Hu (1977) have proposed that the ion gradient across a cell membrane can be altered significantly by applying PW radiation at 10^5 V/m peak field strength or more. This theoretical view derives from consideration of the balance between field-driven and thermal currents. Changes in the time-averaged concentration gradient occur that depend on the square of the field applied across the membrane, but not on the frequency of the applied field. There are larger terms that are frequency dependent but when averaged over a complete cycle are zero. This mechanism has not been demonstrated in a biological system.

Pickard and Rosenbaum (1978) considered a similar problem and came to the same conclusion for the time-averaged concentration gradient across the membrane. In their model, they included unidirectional ion channels through the membrane, and they postulated that the new concentration gradient is achieved by the field-induced movement of ions through these channels. They calculated that, for this particular method of achieving the concentration gradient, the frequency of the field must be < 200 MHz if the ions are protons, and < 10 MHz for less mobile ions. Pickard and Barsoum (1981) have demonstrated activity across the membrane of a plant cell that begins at the onset of an RF field below 10 MHz. The immediate response to the field indicates that the activity is not thermally induced. The activity demonstrated is consistent with an RF-induced DC potential across the membrane. This potential could result from any nonlinear response of the membrane to the RF field, and it is not clear that any particular mechanism for that response has been demonstrated. More data are needed to demonstrate a realistic microscopic model for this process. It is difficult to proceed from these mathematical models and this single experimental demonstration to an assessment of the importance of this mechanism. The induction of DC or extra-low-frequency potentials in biological systems by an RF field could provide significant mechanisms for the biological effects of RF radiation.

3.3 EXPERIMENTAL METHODS

Claude M. Weil

Joseph S. Ali

3.3.1 Exposure Methods Used in Biological Experimentation

In this section the most commonly used exposure methods employed in RF biological effects research are reviewed, and the inherent advantages and disadvantages of each discussed. Researchers have used a diversity of exposure methods, the chosen method having depended on the specialized application involved, the existing facilities available for experimentation, and the cost of setting up new facilities. This diversity may have created difficulties in reproducing biological effects studies, which have, in turn, fueled controversies on several reported effects. Whereas an effect may have been noted by one group who employed a particular form of exposure system, a second group that carefully reproduced the experiment in every detail but for the exposure method might not see the reported effects. It is possible that basic differences in the exposure environment may, in some cases, explain this lack of reproducibility.

In much of the literature, effects have been traditionally reported as a function of incident power density, the independent variable. As pointed out by several prominent workers (King *et al*. 1970; Johnson 1975), power density is an inadequate and inappropriate independent variable for two reasons:

1) Biological effects are logically related to localized or whole-body RF absorption, which is in turn a nonlinear and complex

function of frequency vs. body size, body shape, and orientation to field vectors, etc. (See § 3.2, RF Field Interactions with Biological Systems.)

2) Although meaningful for certain plane-wave-exposure situations, such as free-field or transverse electromagnetic (TEM)-mode cells, the power density concept is no longer applicable in most other commonly used exposure systems with complex irradiation fields. Consequently, meaningful comparisons of the incident field levels in different types of exposure systems cannot be made on this basis.

For these reasons, it must be concluded that the various exposure methods are unique; experimental results obtained in different exposure environments cannot be compared except perhaps on a whole-body-averaged SAR basis, and reproducibility of experimental data is not guaranteed unless exactly the same exposure methodology has been used. Even if equivalency of whole-body-averaged SAR is achieved, there may still be differences in biological outcomes for exposures performed in multipath fields (e.g., a cavity) when compared to plane-wave fields, which have the same carrier frequency and modulation parameters.

Although many of the specialized requirements of a particular experiment are unique, some requirements are common to almost all experiments. For example, there is a critical need in virtually all work for temperature and humidity regulation of the environment in which animals, biological specimens, etc., are located. This ensures that the ambient air temperature and humidity are properly controlled, thereby minimizing the possibility of unwanted variability in the experimental protocol. Two other important requirements are common to the majority of experiments involving whole-body or unrestricted irradiation of animals: (1) an animal population large enough to allow for statistically reliable conclusions to be drawn, and (2) an equally large population of control animals that must be housed during exposure periods under conditions that are, in every way, virtually identical to those of irradiated animals except for the presence of RF energy. For certain critical experiments, there may also be a need for a population of passive or reference control animals that are maintained under normal conditions in their vivarium during the tenure of a study. Much of the early experimental work on RF biological effects frequently contained no provision for controls, involved inadequate numbers of experimental subjects, and lacked adequate provision for environmental control, thus yielding data of questionable validity. It is only within the past decade or so that researchers have succeeded in correcting most of these experimental deficiencies in exposure protocol.

Existing exposure methods have been reviewed by Weil (1977) and Ho et al. (1976); the latter paper discusses exposure techniques that have been used at the FDA's Bureau of Radiological Health. The commonly used methods are categorized into two groups and considered separately: (1) free-field, and (2) enclosed. In the former category, the exposure fields are generated within a reflection-free environment by a radiating antenna or applicator, whereas in the latter category, the exposure fields are those excited within a structure of reflective or conducting walls.

3.3.1.1 Free Field--

Free-field exposure methods were historically the first to be used in such experimentation and remain the most commonly used techniques. These methods involve placing the experimental subject(s) in the near-field or far-field region of a radiating antenna, such as a horn, parabolic dish, or diathermy applicator. For exposures in the far-field region, all unwanted scattering of RF energy from the surrounding room structure, etc., must be eliminated. Otherwise, the power density levels at the subject's location are not well established. This requires using microwave-absorbing material that wholly or partially surrounds the experimental subjects, creating what is termed an anechoic chamber. (The term "anechoic," meaning "without echoes," has been borrowed from acoustics research.) The design of anechoic chambers is a specialized art normally performed by commercial manufacturers of absorbing material (e.g., Emerson and Cuming, Canton, MA). The anechoic properties of such chambers, which are defined by the characteristics of the "quiet zone" where the experimental subjects are placed, is a function of the reflective properties of the absorbing material with which the chamber is lined. (Such properties refer to the degree with which RF energy is reflected by the material, rather than absorbed.) Reflectivity is proportional to the incident wavelength so that the performance of an anechoic chamber will markedly deteriorate as the frequency of operation is lowered. A minimum reflectivity of 20 dB (1 percent) is usually considered essential; the frequency at which this value is reached then defines the lower frequency limit of operation for the chamber. Anechoic chambers perform well at frequencies in the microwave region of the spectrum (above 500 MHz). However, satisfactory performance at lower frequencies or longer wavelengths requires using large blocks of absorbing material formed into long pyramids or cones. Consequently, a large structure is needed to house such a chamber, so that the cost of such a facility rapidly escalates to the point of nonfeasibility. For all intents and purposes, it is impractical to contemplate building anechoic facilities that operate at frequencies below ~ 250 MHz.

Some of the most extensive anechoic chamber facilities devoted to RF biological effects work are to be found at the Department of Microwave Research of the Walter Reed Army Institute of Research, Silver Spring, MD. Similar conventional anechoic facilities are found elsewhere; e.g., at the Bureau of Radiological Health in Rockville, MD, at the U.S. Environmental Protection Agency in Research Triangle Park, NC (Figures 3-15 and 3-16), and at the U.S. Air Force School of Aerospace Medicine in San Antonio, TX.

The principal advantages--applicable to exposures in only the far-field zone of an antenna--of the free-field exposure method are:

- The incident power density to which the subject is exposed can be well defined to an accuracy of ±1 dB (±20 percent) or less. This makes replication of experiments performed under free-field conditions fairly straightforward.
- Depending on the directionality of the radiating antenna, the exposure area where the irradiated subjects are placed is large, and the irradiation is nearly uniform (±10 percent or less).

The principal disadvantages of free-field exposure methods are:

- The facilities are costly and often require extensive floor space.
- Very high-power RF sources are needed to obtain the necessary power density levels. Consequently, many free-field facilities employed in bioeffects research operate on either of two ISM

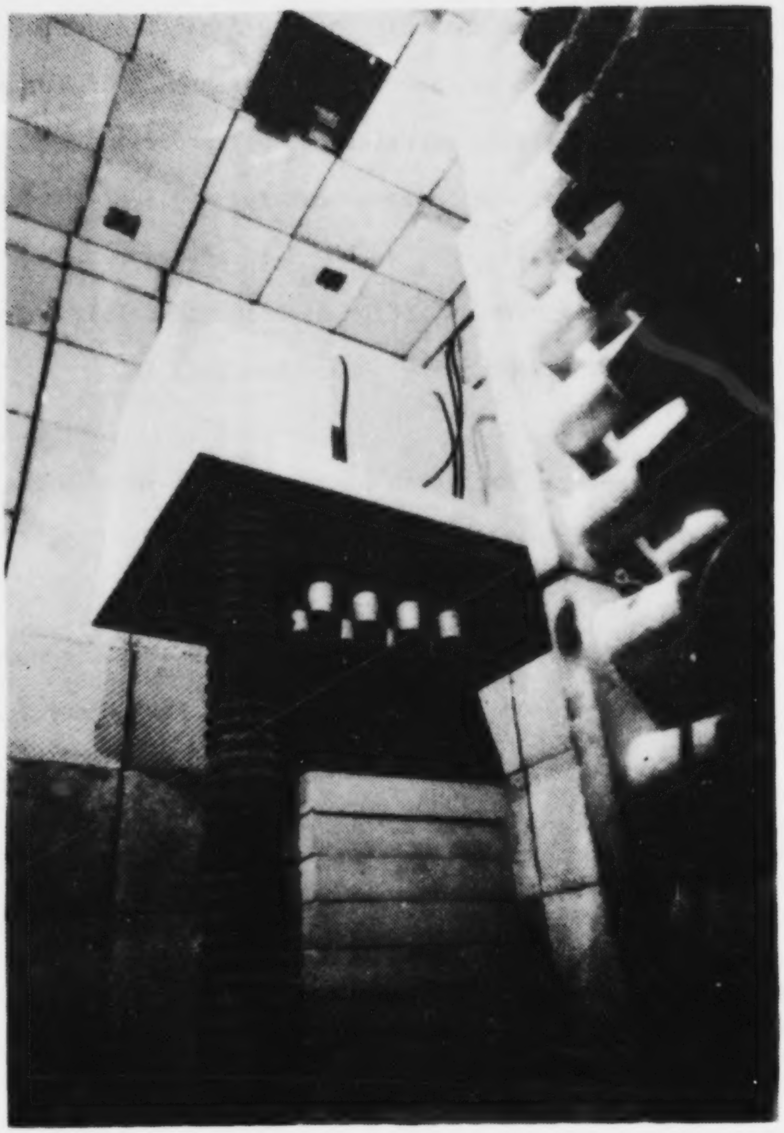


Figure 3-15. EPA 2450-MHz anechoic chamber facility, or 2.45-GHz far-field exposure facility. Horn antenna (top), temperature control chamber (center), and one air duct (bottom left) are visible in the shielded anechoic room (Blackman et al. 1975, Elder and Ali 1975).

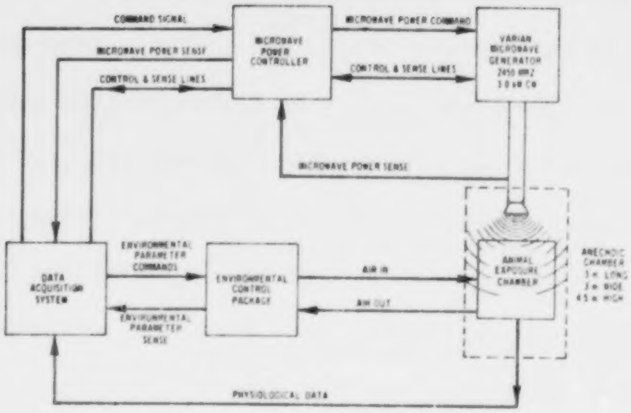

COMMAND SIGNAL
MICROWAVE POWER SENSE
CONTROL & SENSE LINES
MICROWAVE POWER CONTROLLER
MICROWAVE POWER COMMAND
CONTROL & SENSE LINES
VARIAN MICROWAVE GENERATOR 2450 MHZ 3.0 kW CW
MICROWAVE POWER SENSE
DATA ACQUISITION SYSTEM
ENVIRONMENTAL PARAMETER COMMANDS
ENVIRONMENTAL PARAMETER SENSE
ENVIRONMENTAL CONTROL PACKAGE
AIR IN
AIR OUT
ANIMAL EXPOSURE CHAMBER
ANECHOIC CHAMBER 3 m LONG 3 m WIDE 4.5 m HIGH
PHYSIOLOGICAL DATA

Figure 3-16. EPA 2450-MHz anechoic chamber facility: diagram of the microwave exposure facility (Blackman et al. 1975; Elder and Ali 1975).

frequency assignments used for microwave heating, 2450 MHz or 915 MHz, where high power sources are commercially available at relatively low cost. This is why 2450 MHz has become a standard microwave frequency for bioeffects research.

- Free-field systems are an excellent simulation of the idealized exposure concept visualized in many protection standards, but these systems do not represent the real-life exposure situation encountered by humans.
- The whole-body-averaged SAR cannot be measured directly in a free-field situation. Reasonably accurate estimates of the SAR can be made by calorimetric measurements on animal carcasses. (See § 3.4, Dosimetric Methods.)

Various attempts have been made to modify conventional free-field exposure methods to ameliorate the cost and space problems associated with them. A study (Bassett et al. 1971) performed at the Georgia Institute of Technology developed several such techniques. One of these employs the absorber-lined horn antenna, which enables a subject to be placed much closer to the horn aperture than is the case with a conventional horn and yet to remain within the far-field zone of the radiator. This means that a lower power source can be used to create the same power density at the irradiated subject. One of these absorber-lined horns has been used for several years at the National Institute of Environmental Health Sciences in Research Triangle Park, NC (Figure 3-17). Another technique involves the compact range (Figure 3-18), which uses a feed horn to irradiate a large parabolic reflector. The test subject is exposed in the collimated beam region of the reflector. The advantage of this system is that it creates a much larger test volume of nearly uniform field intensity with associated decrease in the anechoic facility size, as well as reduced requirements for absorbing materials. The compact-range technique is used at the Naval Aerospace Medical Research facility in Pensacola, FL.

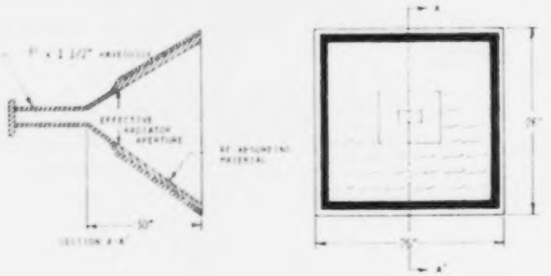


Figure 3-17. Diagram of absorber-lined horn (Bassett _et_ _al_. 1971).

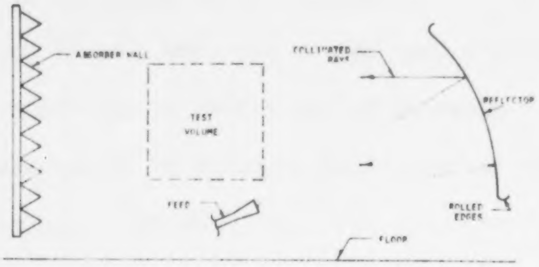


Figure 3-18. Diagram of a point-source compact range (Bassett _et_ _al_. 1971).

As discussed earlier, a critical need in whole-body exposure of animals is to expose large numbers of animals. Consequently, in many experiments, unrestrained animals have frequently been placed inside an anechoic chamber in a closely spaced matrix for simultaneous exposure. This practice tends to obviate the principal advantage of free-field exposure methods, because the power density to which the animal is exposed can no longer be accurately defined due to RF-energy scatter from one animal to another. The degree of scatter is dependent on much the same factors as is absorption (see § 3.2.1) and will vary randomly as the animals constantly alter their relative posture and orientation. Interanimal scatter is most serious when the frequency of exposure lies in the resonant and supraresonant region. Several solutions to this problem have been devised:

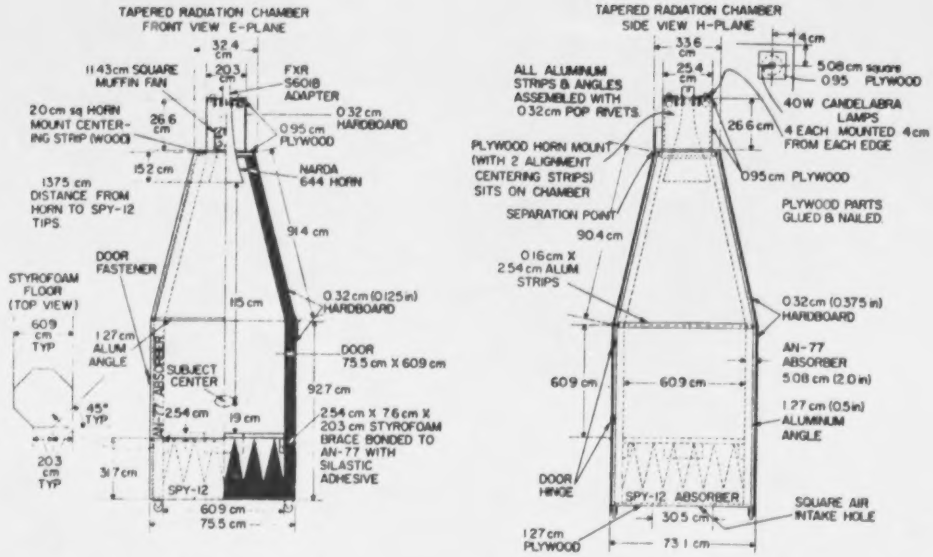
(a) Sequential exposures of single animals in the same free-field facility

(b) Miniature anechoic chambers for exposing animals individually

(c) Separating the restrained animals so that they are spaced one or more wavelengths apart

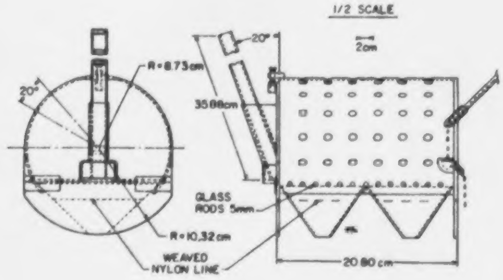
The first solution is obviously costly and time-consuming, and may not be acceptable in certain critical biological experiments requiring all animals to be exposed at exactly the same age or the same time of day, etc. The second solution has been advanced by Guy (1979) at the University of Washington, Seattle. He has described a system of 16 miniature anechoic chambers designed for chronic low level (< 10 mW/cm^2) exposure of rabbits and rodents at 2450 MHz; eight of these chambers are energized, while the other eight serve as control chambers (Figure 3-19). A similar chamber has been constructed at EPA (Figure 3-20). Such a system has, of course, the advantage of ensuring total RF isolation between animals, and, although costly, it may be more economical in cost and power requirements than is the conventional anechoic chamber.

The third solution has been tried by a few workers and appears to be a reasonable compromise between the conflicting requirements of adequate isolation and low cost. Oliva and Catravas (1977) have described a method for simultaneously exposing 10 animals in a conventional anechoic chamber with minimal field interaction between animals (Figure 3-21). The animal cages are located on the antenna beam's three-dimensional contour of constant power density, with cages separated by ~ 2.5 wavelengths at 2450 MHz. The authors claim that the average variation of power density from one cage location to another does not exceed ±5 percent. The major disadvantage of this technique is that its implementation may require a large exposure volume, which, in turn, creates costly problems of ensuring satisfactory environmental control. D'Andrea _et_ _al_. (1979, 1980) at the University of Utah have developed an


TAPERED RADIATION CHAMBER
FRONT VIEW E-PLANE
32 4 cm
20 3 cm
11 43cm SQUARE MUFFIN FAN
FXR S601B ADAPTER
20cm sq HORN MOUNT CENTERING STRIP (WOOD)
26 6 cm
0 32 cm HARDBOARD
0 95 cm PLYWOOD
15 2 cm
NARDA 644 HORN
137 5 cm DISTANCE FROM HORN TO SPY-12 TIPS
91 4 cm
DOOR FASTENER
STYROFOAM FLOOR (TOP VIEW)
115 cm
0 32 cm (0 125 in) HARDBOARD
60 9 cm TYP
1 27cm ALUM ANGLE
AN-77 ABSORBER
SUBJECT CENTER
DOOR 75 5 cm X 60 9 cm
92 7 cm
45° TYP
2 54 cm
19 cm
2 54 cm X 7 6 cm X 20 3 cm STYROFOAM BRACE BONDED TO AN-77 WITH SILASTIC ADHESIVE
20 3 cm TYP
31 7 cm
SPY-12
60 9 cm
75 5 cm
TAPERED RADIATION CHAMBER
SIDE VIEW H-PLANE
33 6 cm
25 4 cm
4cm
5 08cm square
0 95 PLYWOOD
ALL ALUMINUM STRIPS & ANGLES ASSEMBLED WITH 0 32cm POP RIVETS.
40W CANDELABRA LAMPS
26 6 cm
4 EACH MOUNTED 4cm FROM EACH EDGE
PLYWOOD HORN MOUNT (WITH 2 ALIGNMENT CENTERING STRIPS) SITS ON CHAMBER
0 95cm PLYWOOD
SEPARATION POINT
PLYWOOD PARTS GLUED & NAILED
90 4 cm
0 16cm X 2 54 cm ALUM STRIPS
0 32cm (0 375 in) HARDBOARD
AN-77 ABSORBER 5 08 cm (2 0 in)
60 9 cm
60 9 cm
1 27 cm (0 5in) ALUMINUM ANGLE
DOOR HINGE
SPY-12 ABSORBER
SQUARE AIR INTAKE HOLE
30 5 cm
1 27cm PLYWOOD
73 1 cm

a) Construction details of tapered exposure chamber.

b) Construction details of tapered exposure chamber.


1/2 SCALE
2cm
20°
20°
R = 8.73cm
35 88cm
GLASS RODS 5mm
R = 10.32 cm
WEAVED NYLON LINE
20 80 cm

c) Construction details of cage for housing rat in tapered exposure chamber.

Figure 3-19. Miniature anechoic chamber facility (Guy 1979).

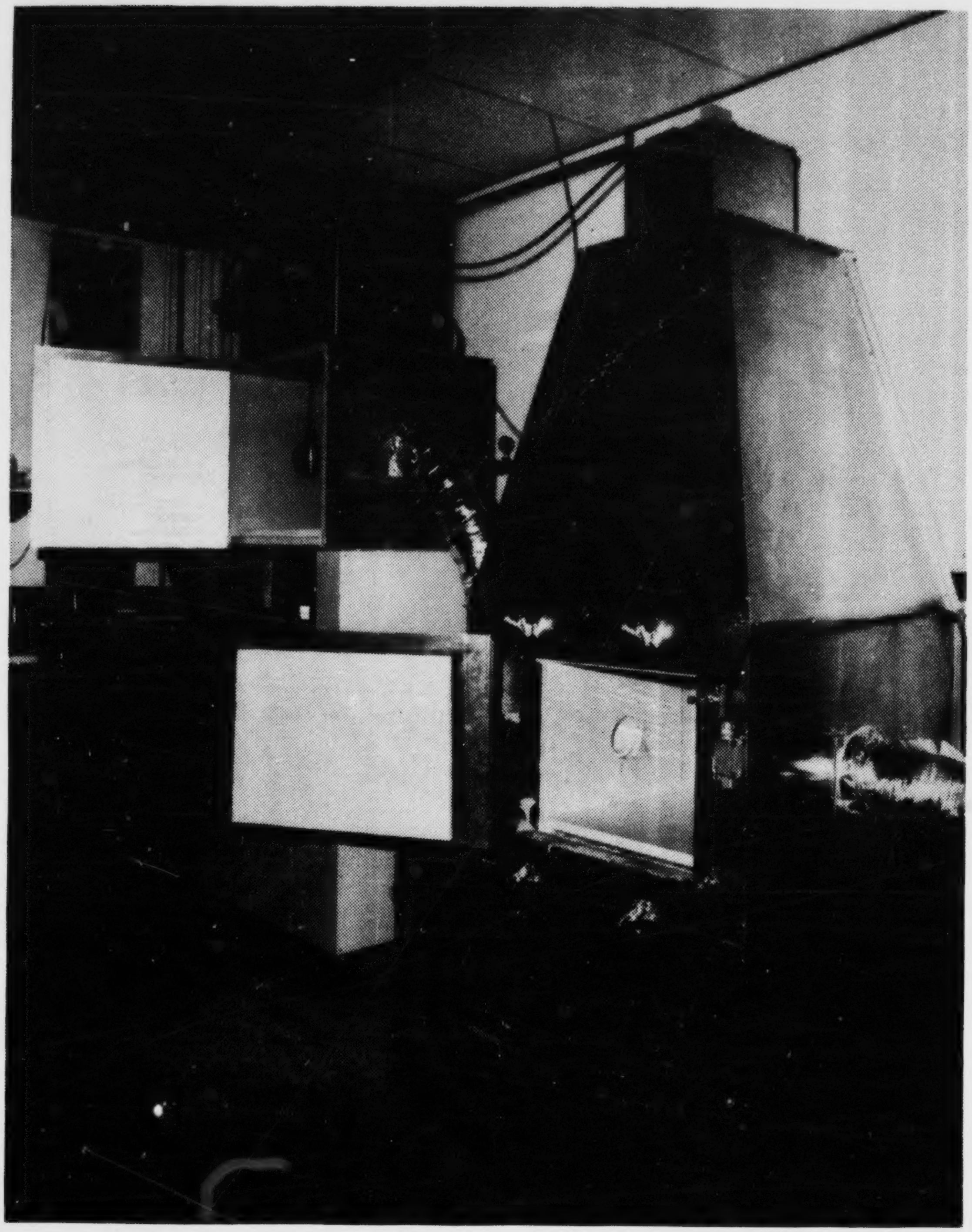
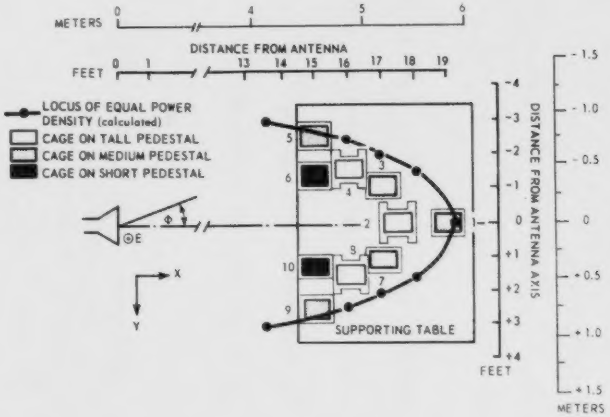
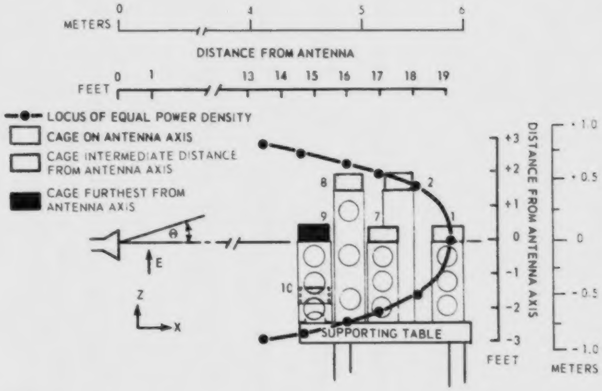


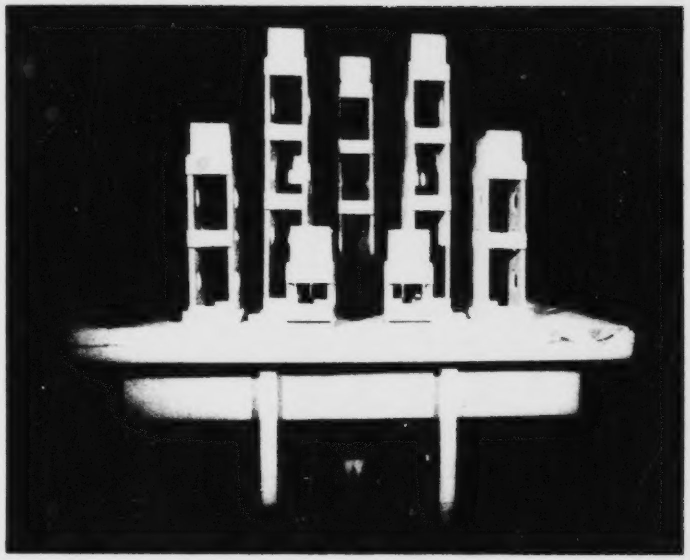
Figure 3-20. Photograph of tapered exposure chamber at EPA facility.


METERS
0
4
5
6
DISTANCE FROM ANTENNA
FEET
0
1
13
14
15
16
17
18
19
LOCUS OF EQUAL POWER DENSITY (calculated)
CAGE ON TALL PEDESTAL
CAGE ON MEDIUM PEDESTAL
CAGE ON SHORT PEDESTAL
Φ
E
X
Y
1
2
3
4
5
6
7
8
9
10
SUPPORTING TABLE
DISTANCE FROM ANTENNA AXIS
-4
-3
-2
-1
0
+1
+2
+3
+4
FEET
-1.5
-1.0
-0.5
0
+0.5
+1.0
+1.5
METERS

a) Locus of equal power density in the H plane through the axis of the transmitting antenna.


METERS
0
4
5
6
DISTANCE FROM ANTENNA
FEET
0
1
13
14
15
16
17
18
19
LOCUS OF EQUAL POWER DENSITY
CAGE ON ANTENNA AXIS
CAGE INTERMEDIATE DISTANCE FROM ANTENNA AXIS
CAGE FURTHEST FROM ANTENNA AXIS
Θ
E
Z
X
1
2
7
8
9
10
SUPPORTING TABLE
DISTANCE FROM ANTENNA AXIS
+3
+2
+1
0
-1
-2
-3
FEET
+1.0
+0.5
0
-0.5
-1.0
METERS

b) Locus of equal power density in the E plane through the axis of the transmitting antenna.



c) Multiple-animal array for equal power density microwave irradiation.

Figure 3-21. Facility for simultaneous exposure of 10 animals with minimal inter-animal interaction (Oliva and Catravas 1977).

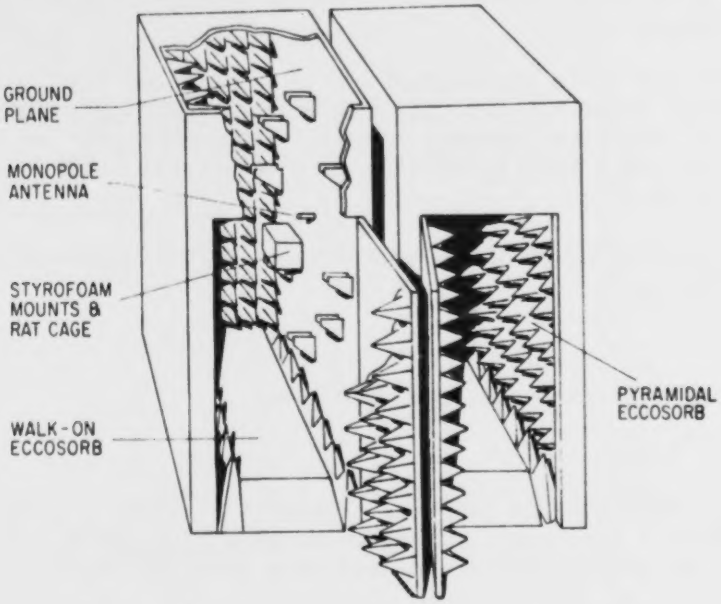
alternate method involving a monopole radiator on a vertical ground plane. The animals are located next to the ground plane on a circular locus that is centered at the monopole (Figure 3-22). Each circular array contains 10 animals that are separated by ~ 5.5 wavelengths at 2450 MHz, and by 2.1 wavelengths at 915 MHz. This system offers the advantage of reducing both space and RF-power requirements. Furthermore, the presence of a ground plane makes this system more representative of the real-life exposure situation for humans. On the other hand, the exposure characteristics of this system may not be comparable to a conventional anechoic chamber facility, so that caution is needed when comparing data.

For situations involving the exposures of only one subject at greatly increased power density values, D'Andrea *et al*. (1977) and Hagmann and Gandhi (1979) have discussed a modification of this system in which a corner reflector is placed behind the monopole. By placing the subject 1.5 wavelengths from the corner point, it is possible to obtain an SAR enhancement of more than 20 times relative to that obtained without the reflector.

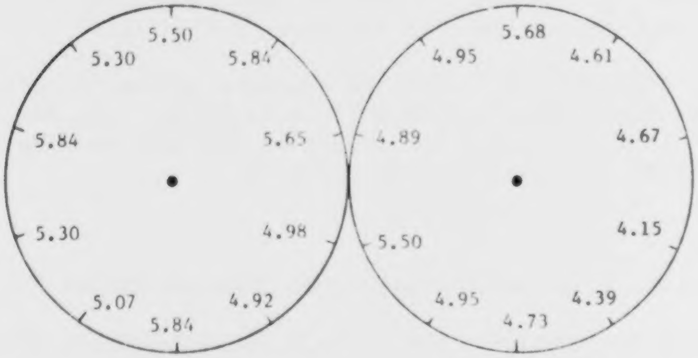
3.3.1.2 Enclosed Systems--

Enclosed exposure systems are those in which the EM fields are contained within a conducting structure. These fall into two basic subcategories, which are considered separately: (a) transmission line systems, and (b) cavity systems. The principal advantages of enclosed systems are as follows:

- By suitable monitoring of the incident, reflected, and transmitted power in the exposure system, more accurate SAR estimates can be made for the exposed subject than is possible in free-field


GROUND PLANE
MONOPOLE ANTENNA
STYROFOAM MOUNTS & RAT CAGE
WALK-ON ECCOSORB
PYRAMIDAL ECCOSORB

a) Representation of the microwave-exposure chamber.


5.50
5.30
5.84
5.84
5.65
5.30
4.98
5.07
4.92
5.84
5.68
4.95
4.61
4.89
4.67
5.50
4.15
4.95
4.39
4.73

Left chamber

Mean mW/cm^2
5.42 ± .21

Right chamber

Mean mW/cm^2
4.85 ± .27

SAR - mW/g
1.23 ± .25
(n = 3)

b) Distribution of power densities measured at each rat's location within the Plexiglas holding cages for both sides of the microwave exposure chamber in the absence of the rats. (2450 MHz)

Figure 3-22. Monopole-over-ground plane irradiation facility (D'Andrea et al. 1979, 1980).

facilities. The accuracy in estimating SAR depends in part on how much base-line power loss there is for the unloaded system and to what extent this is affected by the presence of the exposed subject.

- The cost and space requirements of such a system are usually lower than those for free-field methods, depending on the number of identical systems needed. Also, much smaller and less expensive power sources will suffice to establish the same field intensities.
- Better control of RF absorption in the irradiated subject is possible.

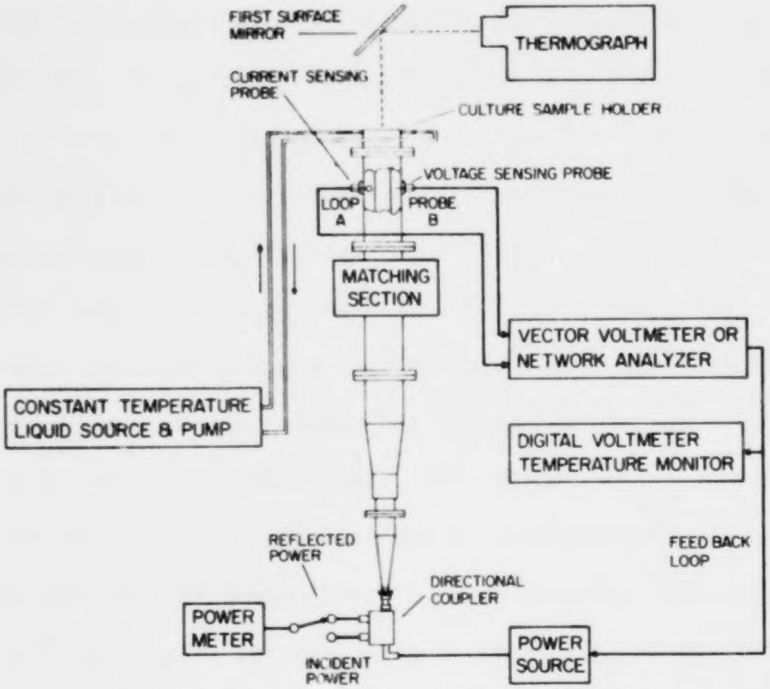
The principal disadvantages are as follows:

- With the exception of TEM-mode transmission lines (to be explained), the fields are complex and not plane-wave equivalent, thereby making comparison with free-field data more difficult.
- With the exception of multi-modal systems (also to be explained), the exposure space available inside such systems is limited. Although the available space may be adequate for small animals such as rodents, it may not be possible to fit a rabbit or monkey in it. Thus, the variety of species that can be employed in an existing facility of the enclosed type is restricted.
- The field distribution within the exposure system is rarely as uniform as that found in a free-field facility. The field distribution is well defined for single or dominant mode operation, but undefined for multiple-mode operation.

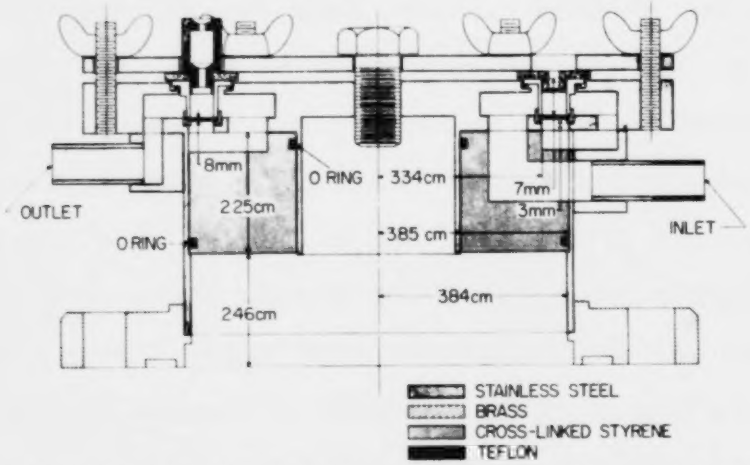
Enclosed systems have been the preferred exposure method for samples, specimens, *in vitro* preparations, etc., since these materials are small enough to fit easily inside such systems. Many experiments have been described, too numerous to survey here, in which different types of waveguide, TEM-mode lines, and cavities have been used to irradiate such preparations. In recent years, some enclosed-type systems have been specifically designed for whole-body irradiation of animals. These are discussed here in more detail. Owing to the need to define accurately the field level to which the animal is exposed, dominant-mode operation of these devices has been preferred over multi-mode operation. However, this puts an upper limit on the frequency of operation, depending on the size of the system needed to expose an experimental animal. For example, most of the dominant-mode, enclosed systems that have been used to expose rats operate at frequencies below 1000 MHz; for mice, which require a smaller exposure volume, single-mode operation to ~ 3000 MHz is possible. Since free-field methods of exposure are largely impractical at these lower frequencies, as discussed earlier, enclosed systems do provide experimenters with virtually the only practical and economical method of exposing animals in the HF, VHF, and lower UHF segments of the RF spectrum. A few large-scale systems have been built to operate in the dominant mode at HF and lower VHF frequencies; these are large enough to accommodate a group of animals within the exposure area, and the animal-to-animal interaction problem is minimized because exposures are conducted in the subresonant region where interanimal scatter is minimal. However, at higher frequencies such methods become impractical, and it becomes necessary to provide an identical exposure system for each animal to be irradiated. Each exposure device is fed from a single high-power source by a power dividing network. One of the basic electrical problems associated with any enclosed exposure system is that, when loaded, there is considerable reflection of RF energy from the load, which propagates via feed lines back to the RF power source. This characteristic creates particular problems for multiple systems fed by a single power source because, without sufficient isolation between each exposure device, energy is continuously reflected from one system into the others, causing unwanted fluctuations in the RF energy incident to each system. These problems can be solved by installing isolators in each feed line, thereby preventing the reflected energy from reaching the dividing network and the RF power source. The two categories of enclosed system are discussed separately.

Transmission lines--In these systems, an EM wave propagates down the line from source to termination. When the line is terminated in its characteristic impedance, only the outwardly propagating wave exists with no reflected wave present. (The characteristic impedance is a basic electrical parameter that is defined by the line's configuration and dimensions.) However, if the line is terminated in a short circuit or an open circuit, all of the energy is then reflected at the line's termination. The two systems of traveling waves together create a standing wave that possesses successive maxima of electric and magnetic fields (E and H, respectively) spaced a quarter of a wavelength apart. This property is a useful feature that has been used by some workers to expose specimens or samples to isolated E or H fields, depending on the location along the line. The characteristics of a shorted or open transmission line are similar to those of the resonant cavity, and are discussed below.

Transmission-line devices can be subcategorized into TEM-mode or waveguide. In TEM-mode lines--coaxial air lines, parallel-plate (strip) lines, etc.--the dominant mode of operation is a propagating TEM mode, provided the line is properly terminated in its characteristic impedance. In TEM-mode operation the E- and H-field vectors are mutually orthogonal, and lie only in the plane transverse to the direction of wave propagation. This is seen to be virtually identical to a plane wave, so that it is possible to simulate free-space conditions inside such lines, provided that the exposed subject does not occupy more than about a third of the line's cross-sectional area. (If the one-third restriction is exceeded, ground-plane effects are observed.) Because of its circular cross section, the coaxial air line has been used only with fluid or precut solid samples; the primary application has usually been in making dielectric measurements. A sophisticated coaxial air-line system, designed to expose cell cultures to high field strengths, has been described by Guy (1977) (Figure 3-23). Parallel-plate systems consisting of a conductor located over a ground plane or between two ground planes are better suited to animal exposures since they provide a rectangular volume where animals can be exposed. D'Andrea and Gandhi (1976) have described a simple parallel plate system used in the range 200 to 500 MHz (Figure 3-24). This system is equivalent to a large scale version of a microstrip line with air dielectric. Capacitive-plate devices, which are equivalent to a short length of parallel plate that is terminated in an open circuit, have been used for exposing *in vitro* preparations to isolated electric fields. This type of simple device has been incorporated in a unique HF-band (10- to 40-MHz) exposure system developed by the National Bureau of Standards (Figure 3-25). Termed a near-field synthesizer, it is capable of separate E- and H-field excitation, the latter generated by special loop inductors (Greene 1976). By altering the spatial position of the loop with respect to the E vector and by changing the phase relationship between the signals exciting the plates and the


FIRST SURFACE MIRROR
THERMOGRAPH
CURRENT SENSING PROBE
CULTURE SAMPLE HOLDER
VOLTAGE SENSING PROBE
LOOP A
PROBE B
MATCHING SECTION
VECTOR VOLTMETER OR NETWORK ANALYZER
CONSTANT TEMPERATURE LIQUID SOURCE & PUMP
DIGITAL VOLTMETER TEMPERATURE MONITOR
REFLECTED POWER
FEED BACK LOOP
DIRECTIONAL COUPLER
POWER METER
INCIDENT POWER
POWER SOURCE

a) Complete system for exposing cell cultures to EM fields.


8mm
O RING
334cm
225cm
7mm
3mm
OUTLET
O RING
385 cm
INLET
384cm
246cm
STAINLESS STEEL
BRASS
CROSS-LINKED STYRENE
TEFLON

b) Cross-sectional view of assembled transmission-line cell-culture sample holder and heat exchanger. (A section of the outer conductor is machined to 7.70-cm ID so a 7.71-cm diameter dielectric support can be firmly locked into place after being pressed in while the conductor is heated.)

Figure 3-23. Coaxial air-line system for high power exposures of cell cultures (Guy 1977).

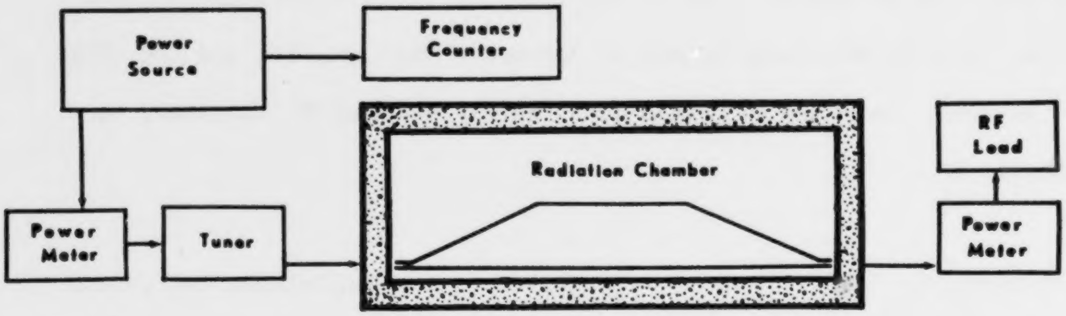

Power Source
Frequency Counter
Radiation Chamber
RF Load
Power Meter
Tuner
Power Meter

Figure 3-24. Parallel-plate (microstrip) exposure system (D'Andrea _et al_. 1976).

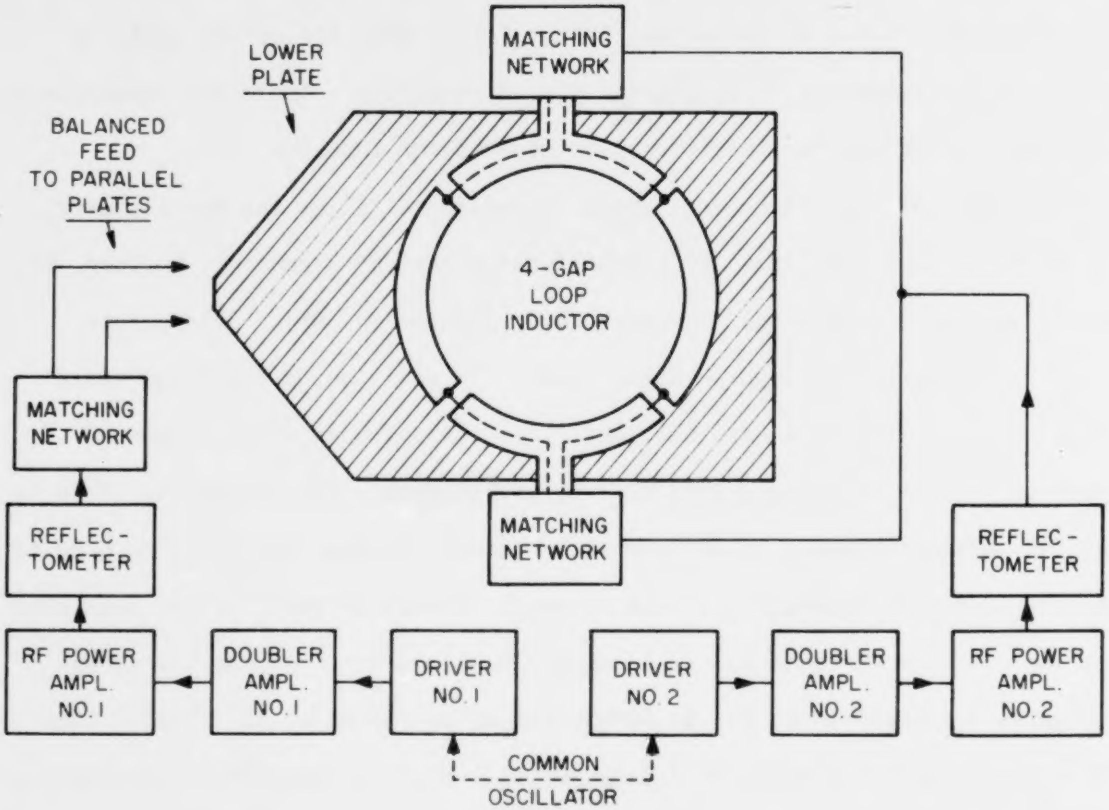

LOWER PLATE
MATCHING NETWORK
BALANCED FEED TO PARALLEL PLATES
4-GAP LOOP INDUCTOR
MATCHING NETWORK
REFLEC-TOMETER
MATCHING NETWORK
REFLEC-TOMETER
RF POWER AMPL. NO. 1
DOUBLER AMPL. NO. 1
DRIVER NO. 1
DRIVER NO. 2
DOUBLER AMPL. NO. 2
RF POWER AMPL. NO. 2
COMMON OSCILLATOR

Figure 3-25. Block diagram of the complete RF near-field synthesizer, showing all principal components including RF power sources.

loop, it is possible to simulate the complex field environment existing in the near-field of an HF source. Two of these systems are presently being used; one is at the U.S. Air Force School of Aerospace Medicine, TX, and the other at the National Institute of Occupational Safety and Health laboratory in Cincinnati, OH.

Triple-plate lines, in which a conductor is mounted between two ground planes, have been used by a few workers. These have the advantage of allowing for simultaneous irradiation of two animals while maintaining good isolation between them. In a more popular version of this system, the open sides of the structure are closed off with two side plates so that the center plate is entirely surrounded by a rectangular ground structure. These are commercially available in different sizes (from Instruments for Industry, Inc., Farmingdale, NY) and have been termed "Crawford cells" by the manufacturer, after M. L. Crawford (1974) of the National Bureau of Standards, Boulder, CO, (also available from Narda Microwave Corp., Plainview, NY). This author prefers the term "rectangular strip line." In addition, a few large-scale facilities of this type have been built for various specialized exposure applications at relatively long (≥ 3 m) wavelengths. The largest of these is at the Defence Research Establishment in Ottawa, Canada, and is being used to measure human RF absorption in the HF band. A smaller facility has been used at the U.S. Air Force School of Aerospace Medicine for exposing infrahuman primates and phantoms to 10- to 50-MHz radiation (Allen et al. 1976). The U.S. Environmental Protection Agency has also built a Crawford-type structure (Figure 3-26) for exposing 20 rats to 100-MHz radiation.

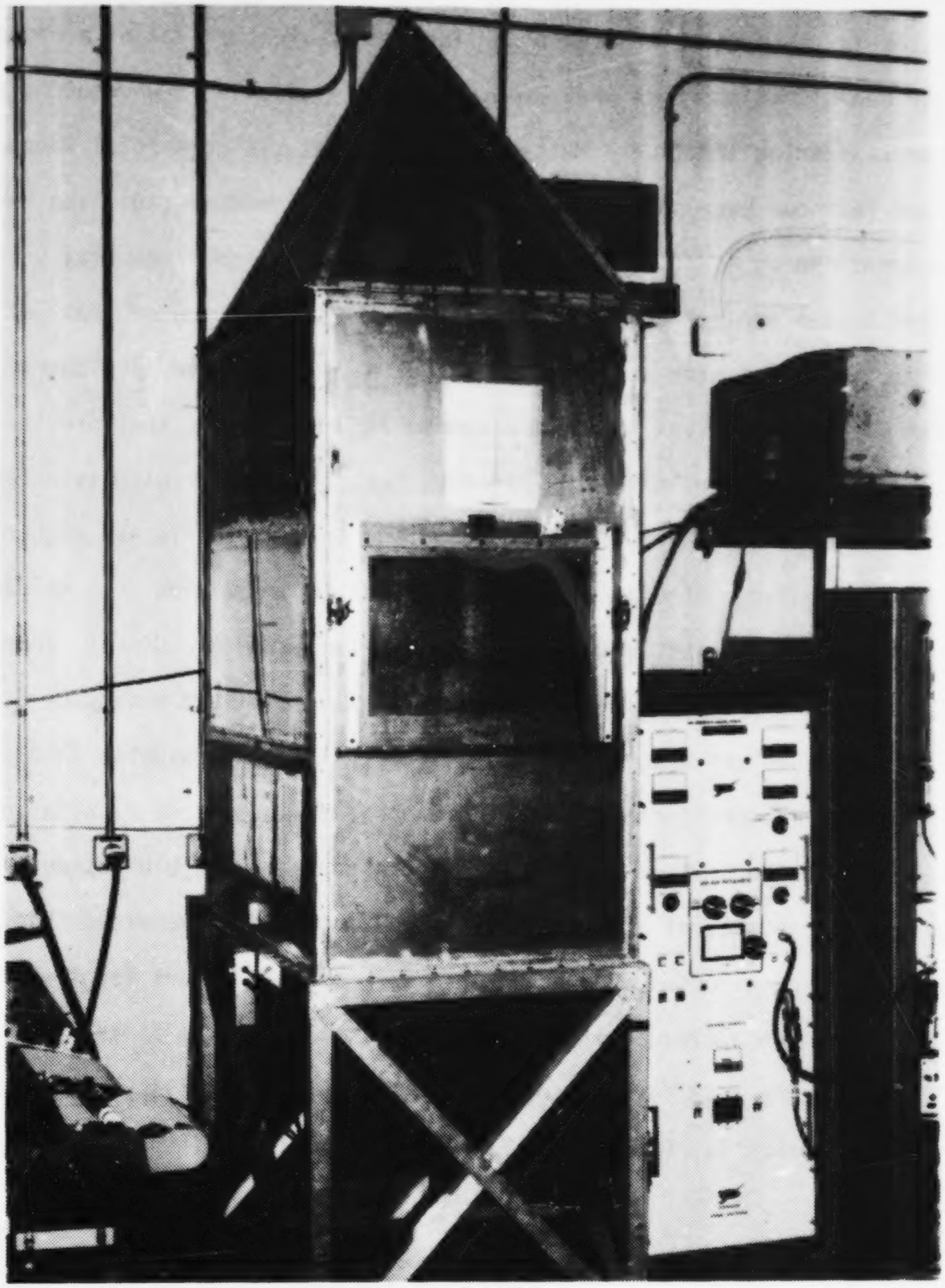


Figure 3-26. EPA 100-MHz rectangular strip line or Crawford cell.

The second category of transmission-line devices, waveguides, cannot support the propagation of a TEM mode so that the incident radiation is inevitably more complex than that in a TEM-mode line. However, the lack of a center conductor means that there is more exposure space available in waveguides than in the corresponding TEM line. Multiple systems that use commercial waveguide systems have not been applied much for animal whole-body irradiation because of high cost. Ho _et_ _al_. (1973) have described a single, environmentally controlled system employing standard S-band rectangular waveguide that has been used in studies of mice at 2450 MHz. Ho _et_ _al_. (1976) have also described a system of six waveguides fed from a common 2450-MHz source that provides simultaneous irradiation of six mice. Besides cost, another problem associated with using standard waveguides for whole-body irradiation is the high mismatch condition created by the presence of an animal in the waveguide. As discussed earlier, this necessitates the use of costly isolation circuitry. This problem has, to a certain extent, been eliminated in a specialized waveguide system developed by Guy and Chou (1976) at the University of Washington in Seattle. Guy's system is specifically tailored for chronic whole-body irradiation of rats for extended periods of time with known and reproducible dosimetry. It consists of a number of 20-cm (8-in) diameter circular waveguides (Figure 3-27), economically constructed from galvanized wire mesh and short lengths of brass tubing, in which a circularly polarized TE_{11} dominant mode is excited at 915 MHz. Figure 3-28 is a photograph of this type of facility. The use of circular polarization (see § 3.1, Electromagnetic Field Theory) has two major advantages:

1) The wide variations in absorption due to constant changes in the animal's orientation are partially reduced so that the energy

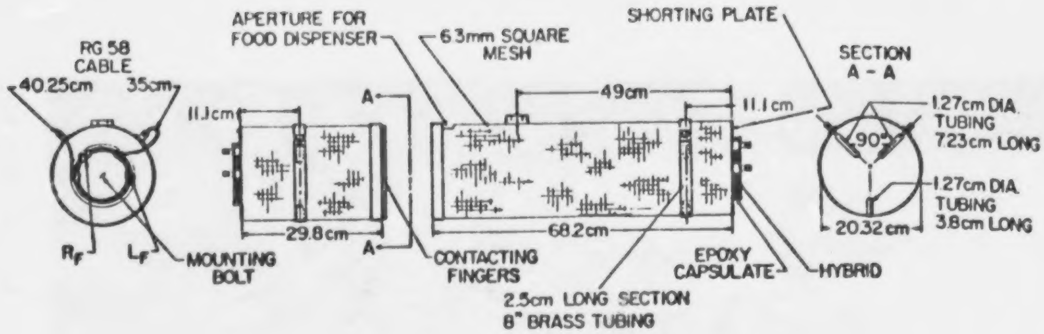

RG 58 CABLE
40.25cm
35cm
R_F
L_F
MOUNTING BOLT
11.1cm
A
29.8cm
A
APERTURE FOR FOOD DISPENSER
6.3mm SQUARE MESH
49cm
11.1cm
SHORTING PLATE
68.2cm
CONTACTING FINGERS
2.5cm LONG SECTION 8" BRASS TUBING
EPOXY CAPSULATE
HYBRID
SECTION A - A
90°
1.27cm DIA. TUBING 7.23cm LONG
1.27cm DIA. TUBING 3.8cm LONG
20.32cm

Figure 3-27. Physical details of the exposure chamber of the circularly polarized 915-MHz waveguide facility (Guy and Chou 1976).

coupled to the animal load remains relatively constant. Note that, whereas in a linearly polarized free-field of perfect field uniformity, the average SAR can vary by ±5-8 dB (±50 percent) at or near resonance, in this system, the average variation of SAR does not exceed ±0.4 dB (±8 percent), even though the incident field uniformity is far from constant.

2) The hybrid coupler used to establish the circular polarization in the waveguide provides a way to isolate reflected from incident energy. This is done by dumping most of the unwanted reflected energy into a load connected to the hybrid, rather than allowing it to return through the power dividing network to the source. This effectively reduces the mismatch normally encountered with loaded waveguides (mean voltage standing wave ratio of less than 1.5:1) and permits parallel operation of multiple units with less isolation circuitry.

Guy et al. (1979) have described a modification of this waveguide system such that it operates in a multimoded field configuration at 2450 MHz. Though it is difficult to define quantitatively the incident energy levels in these

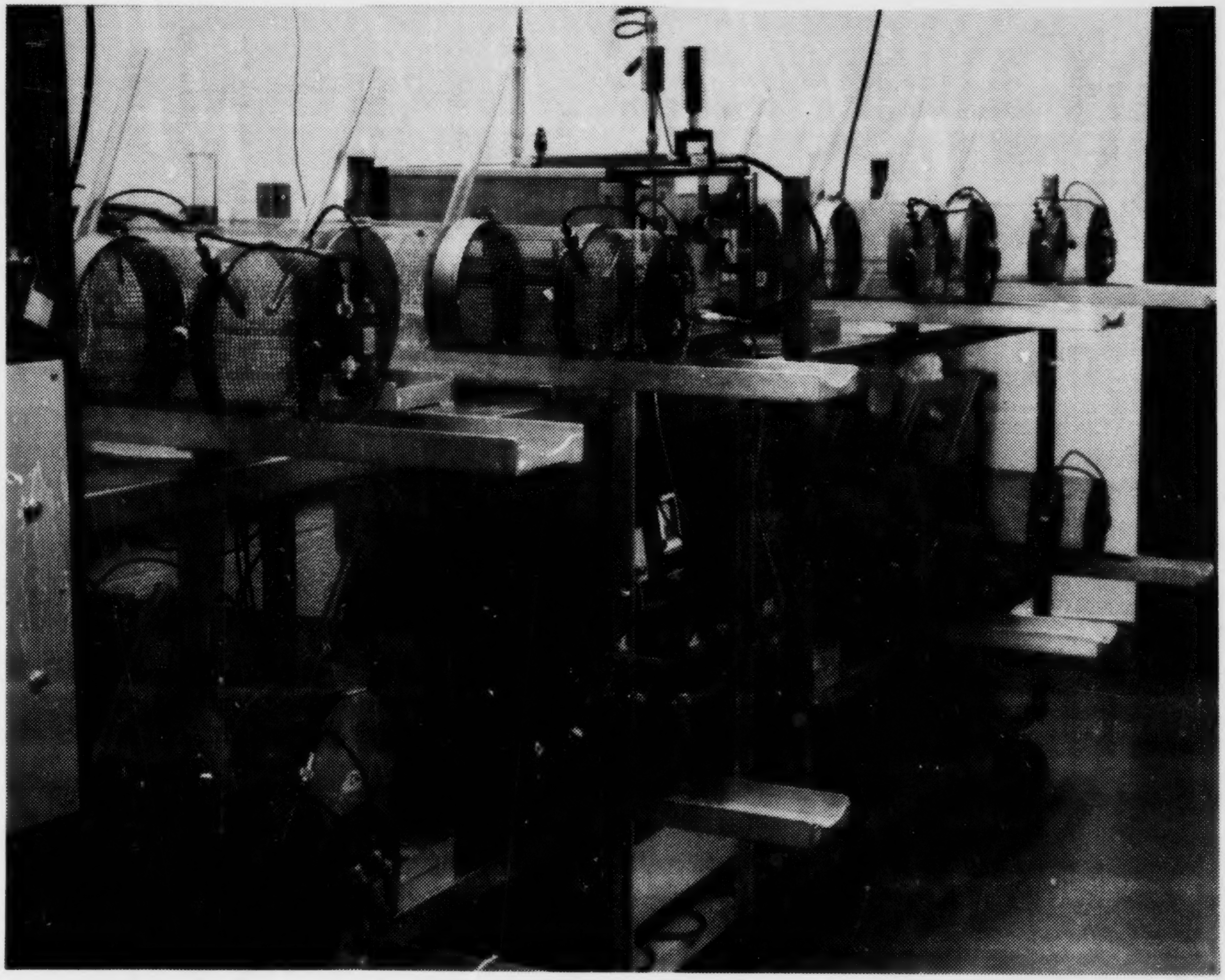
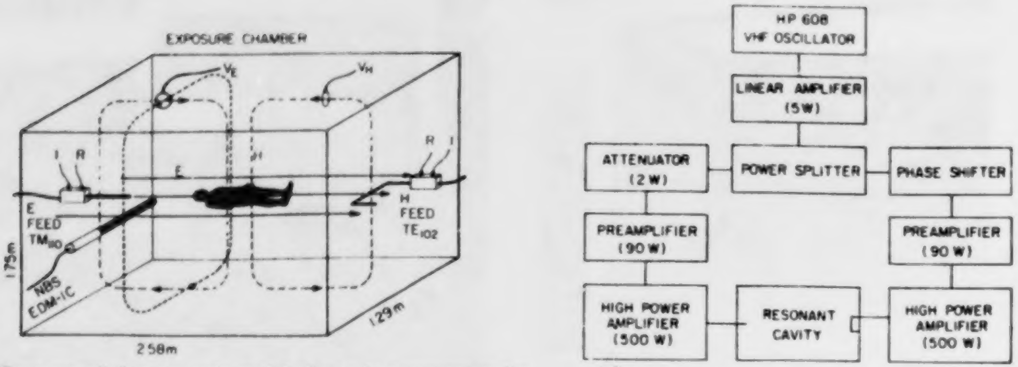


Figure 3-28. Photograph of exposure chamber with associated instrumentation for the 970-MHz circularly polarized waveguide facility at EPA.

units because of the complexity of the fields, the absorption characteristics have been well defined for rats of varying weights. An extensive system of 100 of these units has been installed at Guy's laboratory (Guy et al. 1980) for conducting a chronic radiation study in which rats will be continuously irradiated over a 3-year life span. This study underlines a major advantage of Guy's waveguide systems: animal subjects are able to live continuously in their exposure system with minimal disturbance to their normal living patterns and without artifactual perturbation. Consequently, the system is ideal for the kind of chronic, long term studies that are now being emphasized.

Cavities--The resonant cavity, which is the microwave analog of the lumped-element tuned circuit, consists of a cylindrical, rectangular, or square box with conductive walls. By suitable means, a system of standing waves may be excited within the cavity. By adjusting the cavity dimensions, the system can be made to resonate at the frequency of excitation, such that intense field levels are created within the cavity. The use of the resonant cavity as an exposure device has both a major advantage and disadvantage. A cavity system represents the most efficient way to couple RF energy into a subject per watt of input power; this constitutes its principal advantage. The primary disadvantage is that the field structure within a resonant cavity is probably the most complex to be found in any exposure device. Although some researchers have argued that the field structure within a resonant cavity, particularly when operated multimodally, is a good simulation of the complex multipath environment in which humans are often exposed, it is unlikely that the human exposure environment ever approaches this level of complexity. For the reasons already discussed, the field complexity existing within a cavity makes it difficult to compare experimental data obtained using a particular cavity with those obtained using free-field exposures or even another cavity. Indeed, there are some basic differences between a free-field exposure system and a resonant cavity. For a resonant cavity that is empty (unloaded), or that contains a biological load small in comparison to the cavity's volume (minimal loading), the fields in the cavity are only static and do not propagate. As such, the energy within is only stored. When the loading is greater (i.e., when the exposed subject occupies an appreciable fraction of the cavity's volume) the fields are hybrid, containing both stored and propagating energy. Because the fields are static, minimally loaded cavities are useful for simulating a quasi-static interaction in which object size is small relative to wavelength (i.e., a long-wavelength type exposure). This characteristic has been used by Guy _et al_. (1976), who designed a large rectangular cavity that could be excited either separately or jointly in the TM_{110} or TE_{102} modes at frequencies of ~ 147 MHz (Figure 3-29). This system has been used to study absorption distributions in scaled-down phantom models of man independently exposed to electric or magnetic fields, depending on the mode of excitation. Single-mode circular cavities have also been used by Edwards and Ho (1975) for exposing the head of a monkey at 385 MHz. Guy and Korbel (1972) have discussed the dosimetric aspects of a rectangular cavity used to multiply expose rats at 500 MHz and have sought to emphasize some of the problems associated with cavity exposure systems. Recently, Spiegel _et al_. (1980b) described an interesting variable-volume cavity that contains movable walls such that the cavity can be tuned across a wide frequency range. The system is capable of simultaneously exciting two independent cavity modes and can be used to synthesize complex EM fields.

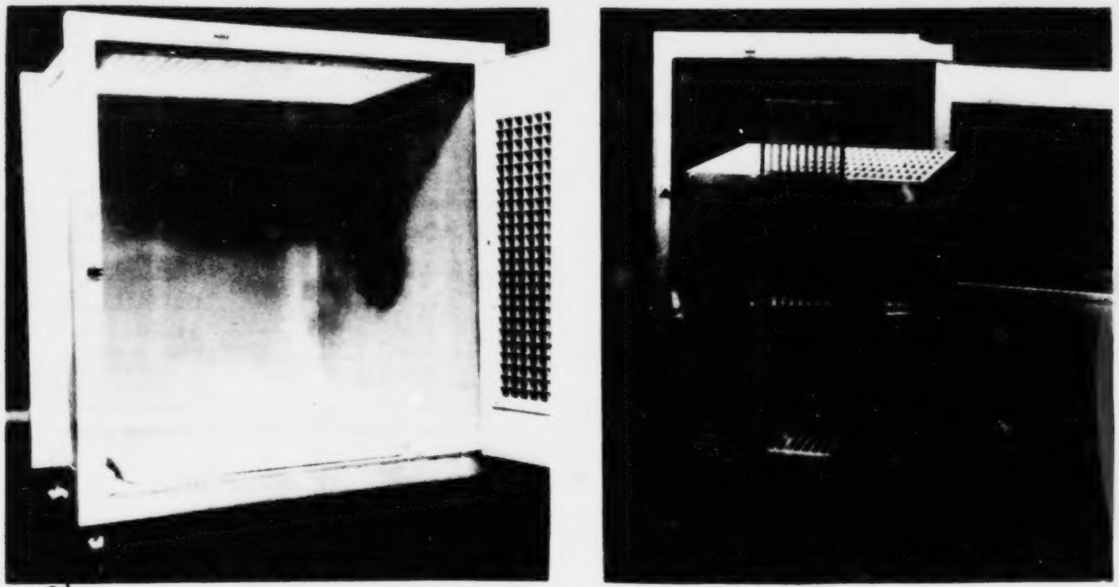

EXPOSURE CHAMBER
V_E
V_H
I R
E
H
R I
E FEED TM_{110}
H FEED TE_{102}
1.75m
NBS EDM-1C
2.58m
1.29m
HP 608 VHF OSCILLATOR
LINEAR AMPLIFIER (5W)
ATTENUATOR (2W)
POWER SPLITTER
PHASE SHIFTER
PREAMPLIFIER (90W)
PREAMPLIFIER (90W)
HIGH POWER AMPLIFIER (500 W)
RESONANT CAVITY
HIGH POWER AMPLIFIER (500 W)

a) Exposure of phantom scale model of man in a resonant cavity.

b) Block diagram of resonant cavity driving system.

Figure 3-29. VHF resonant cavity facility (Guy et al. 1976).

Multimodal cavities, such as microwave ovens, have been used frequently for experimental purposes because of ready availability and modest cost (Justesen et al. 1971). Where ovens have been used, they have been extensively modified to achieve the experimenter's objectives. Multimodal cavities have often been preferred over single-mode types because of the larger exposure volume available and the more uniform field distribution. The latter is achieved by a mode stirrer that helps average-out the field variations within the cavity. The degree of field uniformity achieved in these devices seems to depend greatly on its design. Heynick et al. (1977) have described a multimodal cubical cavity suitable for irradiating nonhuman primates at 2.45 GHz (Figure 3-30). Each unit possesses its own regulated power source. Twelve of these units have been used at SRI International, Menlo Park, CA, to chronically irradiate a group of squirrel monkeys as part of an EPA-sponsored project. Each cavity housed two animals plus offspring.



a) Microwave cavity with door open, showing mode stirrer, iris, radiopaque windows, and waste-collection tray.

b) Dielectric cage.

Figure 3-30. SRI multimodal cavity facility for primate irradiation (Heynick et al. 1977).

3.3.1.3 Conclusions and Unresolved Questions--

There are diverse exposure methods used in biological effects experimentation, most of which differ considerably in their field characteristics. Since each has its own particular advantages and disadvantages, the choice of which system to use has depended on the application. For experiments involving whole-body irradiation of animals, there is a need for some kind of standardized method of exposure on which most researchers can agree. Although such ideas have been proposed and discussed in the past, they are difficult to implement because many exposure requirements are conflicting, and, therefore, no one exposure system can satisfy all of the various requirements. However, some agreement on standardization should enable experiments to be more readily replicated and effects more readily confirmed. Further efforts are needed to this end.

During the past decade, there has been significant improvement in the exposure facilities available for biological experimentation. Many of these facilities have succeeded in overcoming the deficiencies inherent in many of the older exposure devices. Exposure systems specifically designed for chronic irradiation studies must also be developed further, particularly to reduce their cost without significantly sacrificing performance.

There also is a serious need for further studies that compare absorption and biological end points for different forms of exposure. This problem can be summarized as follows: For the same experiment performed in different exposure systems involving plane-wave, complex or multi-path fields, are there differences in biological outcomes even where the same whole-body-averaged SAR is maintained throughout?

3.3.2 Animal Holders

Any experimental irradiation of nonanesthetized animals requires using some form of holder or restrainer to keep the animal in a location of known field strength or power density. For multiple animal exposures, it is also necessary to keep the animals separated from each other. From a dosimetric point of view, the optimal exposure condition is one in which the animal is constrained in one orientation and posture. This way, both whole body and regional dosimetry could be determined with satisfactory precision. However, complete restraint of an animal is considered by most biologists an excessive stress and, therefore, unacceptable. Consequently, the commonly accepted exposure environment represents a reasonable compromise between these conflicting demands: the holder is designed to restrain the animal, allow it to change posture and orientation, and also allow for a small degree of lateral and vertical movement.

3.3.2.1 Perturbation by Restrainers--

One of the important criteria in designing animal holders is that they be constructed of materials that cause the least perturbation of incident fields possible. This means that cages can be built only from nonmetallic materials. Various types of low-loss dielectric materials are available in rigid and semirigid form, and have been the material of choice. The most popular of these has been acrylic plastic (polymethyl methacrylate) because of its optical transparency, superior mechanical strength, and ease of machining. Some experimental and analytical studies have been performed to determine the degree to which these materials perturb the incident field (Weil 1974; Lin et al. 1977). These studies showed that, under certain conditions, these materials can indeed cause serious field perturbations, implying that, in reality, the power density of the field to which the animal is exposed is not known precisely. Using foamed polystyrene instead of acrylic is a possible solution. Foamed polystyrene has a relative permittivity value close to unity and, therefore, creates only minimal field perturbation. There are, however, two disadvantages associated with polystyrene materials: They are optically opaque, so that animals cannot be observed in their cages; they also are not strong and can be readily gnawed by rodents. Coating the material with a substance to which the rodents are averse, such as quinine, has been tried by a few workers (Catravas 1976) to reduce gnawing. However, this practice adds an unwanted additional insult to the experimental subjects. Nonetheless, foamed polystyrene does have application for studies involving short-term exposures.

A more recent paper by Ho (1978) questioned the significance of the incident field perturbations created by holders made of acrylic materials. In an analytical study involving a two-dimensional model that contained a cylinder of muscle-equivalent material mounted concentrically inside an acrylic cylinder, Ho showed that despite a significant perturbation of the incident field in the empty holder, there was relatively little perturbation in the whole-body-averaged SAR and the SAR distribution inside the muscle-equivalent cylinder when compared with that which exists when no holder was present. Ho, therefore, concluded that large field perturbations created by animal holders do not automatically create a correspondingly large perturbation in the animal's absorption rate because the presence of a mass of lossy dielectric (i.e., the animal) tends greatly to damp-out the standing wave patterns created by the acrylic holder. Further experimental observations are needed to confirm this conclusion.

As part of a behavioral investigation, Gage *et al*. (1979) investigated the influence of two different holders on the whole-body SAR of rats and mice at 2450 MHz. One holder was a cuboidal container made of foamed polystyrene, and the other was an acrylic cylinder. They concluded that there was a significant alteration of SAR values for both rats and mice due to the presence of the acrylic cylinder when the animals were oriented parallel to the E-field. This effect was considerably more pronounced in the mouse, probably because 2450 MHz is a frequency close to resonant absorption for the E-parallel orientation of the mouse.

3.3.2.2 Feeding and Watering During Exposure--

Experiments involving chronic, long-term RF irradiation of animals usually require that some arrangements for food and water be made during irradiation. Provision of food does not present difficulties if the standard form of dry food pellets fed to laboratory animals is used, since these absorb little RF energy. However, providing drinking water or liquid nutriment does present some problems because water is a comparatively good conductor and, therefore, absorbs energy. Two methods of supplying water have been used, and each has associated problems.

In the first, the water reservoir is placed in the exposure system with the animal. The major disadvantage here is that, since the water supply is located in a high-field-strength environment, it will absorb RF energy and will perturb surrounding fields. These factors will create uncertainty in both dosimetric and densitometric measurements. Furthermore, it is conceivable that, if the field levels are intense enough, the water temperature could become sufficiently high that the animal would refuse to drink. Consequently, this approach is not recommended.

The second method involves placing the reservoir outside the exposure system in a region of little or no field strength, and supplying water to the animal via a supply tube or pipe. This method is superior, but it, too, has associated pitfalls which, without special precautions, can introduce serious experimental artifacts. As Guy and Chou (1976) have pointed out, the water tube or pipe provides a conductive pathway for microwave currents. When the animal attempts to drink, a circuit is closed between the animal, which is at high potential, and the water reservoir, which is at zero or ground potential. At this time, RF currents will pass from the animal to the watering system; because the contact point area is small and involves sensitive tissue, a high current density may exist in the animal's tongue. Since the animal will find this condition aversive, it will probably refuse to drink. Therefore, the RF current flow through the water supply system must be interrupted. Three methods of interruption have been devised: (a) When the animal interrupts a beam of light using a tongue-licking operant, a small bolus of fluid is injected into the animal's mouth (King _et al_. 1970); (b) the animal holder is equipped with a small water trough which is continuously supplied through a water drip system; and (c) an RF-choke assembly is placed between the animal and the water reservoir to effectively decouple the animal from the water supply when drinking (Figure 3-31). In the choke assembly design (applying only to enclosed systems), water is supplied through copper tubing that forms the center conductor of a shorted quarter-wave section of a triaxial air-line. To prevent the animal from coming into contact with the copper tubing, a short section of glass or acrylic tubing is mounted at its tip. The choke assembly effectively provides a high impedance at the point of animal contact, thereby reducing the RF current in the watering system to near zero.

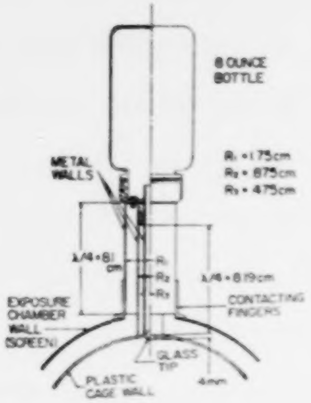

8 OUNCE BOTTLE
R₁ = 1.75cm
R₂ = .875cm
R₃ = .475cm
METAL WALLS
λ/4 = 8.1 cm
R₁
R₂
R₃
λ/4 = 8.19cm
CONTACTING FINGERS
EXPOSURE CHAMBER WALL (SCREEN)
GLASS TIP
PLASTIC CAGE WALL
4mm

Figure 3-31. Water-supply system for exposure chamber (Guy and Chou 1976).

3.3.3 Densitometric Instrumentation

Densitometry is the measurement of RF-field strength and is usually expressed in units of equivalent plane-wave power density. Dosimetry is the measurement of absorbed energy, or the rate of energy absorption by some object in an RF field. In this section, the strength or intensity of an RF field are quantified by measuring a suitable field variable. The question of what constitutes a suitable variable has been addressed (Bowman 1970). For a linearly polarized, plane-wave, EM field in free space--and, for practical purposes, in air--the following relationships exist between the electric field, the magnetic field, the power density, the electric energy density, and the magnetic energy density:

$$\frac{E}{H} = Z_o \qquad (3\text{-}12)$$

$$Z_o = (\frac{\mu_o}{\varepsilon_o})^{1/2} \qquad (3\text{-}13)$$

$$S = \frac{E^2}{Z_o} = Z_o H^2 \qquad (3\text{-}14)$$

$$U = 1/2\ (\varepsilon_o E^2 + \mu_o H^2) = U_E + U_H \qquad (3\text{-}15)$$

$$U_E = U_H \qquad (3\text{-}16)$$

where E = electric field, V/m

H = magnetic field, A/m

Z_o = characteristic or intrinsic impedance of free space, 377 Ω

μ_o = permeability of free space, H/m

ε_o = permittivity of free space, F/m

S = power density, W/m^2

U = total energy density, J/m^3

U_E = electric energy density, J/m^3

U_H = magnetic energy density, J/m^3

The quantities μ_o and ε_o are properties of the medium and are scalar constants for free space. Equation 3-12, therefore, states that the magnitudes of E and H are related by a constant factor Z_o for free space. Equation 3-14 relates the power density S to the individual field components E and H for the basic plane wave. Equation 3-15 is a general relationship for the total energy density U of an RF field, and it defines the individual electric- and magnetic-field energy densities U_E and U_H.

The relationships between field variables for a plane wave are simple, so that the measurement of any one field parameter allows calculation of the others. Although power density is a variable of interest in biological effects studies, it is particularly difficult, if not impossible, to measure directly because it is a time-averaged vector cross product that, in general, is not expressed as simply as Equation 3-14. It may, however, be indirectly evaluated for plane waves by measuring the E or H field, as indicated by Equation 3-14. This measurement, when converted to units of power density (W/m^2) using Equation 3-14, is referred to as the "equivalent plane-wave power density." Above 1 GHz, it is usually not necessary to measure both the E and the H fields (Bowman 1970), whereas below ~ 300 MHz, the H field becomes increasingly important, and an independent measurement of H is necessary (Aslan 1979; Lin et al. 1973).

Power density is, however, inappropriate to use in evaluating near fields of antennas or fields near reflecting surfaces because intense fields can exist in these regions while the power density is low or even zero. A plane wave normally incident on a conducting surface can create standing waves with large E and H values but very low power density. Since power density is a measure of the power flow across a unit area, the net power flow of a plane wave normally incident on a conducting surface and reflecting back is zero (or small in practical cases), and hence the power density is zero. The E and H fields will now be in a standing-wave pattern with amplitudes twice those of the fields of the incident wave.

In the near field of sources or for complex RF fields, the E and H fields are not related by Equation 3-12; however, Equation 3-15, which relates the individual E and H fields to their respective energy densities, is always true. Therefore, measurements of both the E and H fields are required to evaluate the total energy density where Equation 3-12 does not apply.

Bowman (1970), Swicord (1971), and others have described the desirable characteristics of an instrument for quantifying hazardous EM fields. The instrument and probe should: 1) measure in terms of energy density and respond only to the variable being measured, 2) be small to permit a high degree of spatial resolution and thus be useful in small volumes, and 3) should have an isotropic response and be insensitive to field polarization. The probe should also cause little scattering of the field and operate over a broad frequency range. The instrument and probe should be battery powered, lightweight, and rugged, and should read either peak or average values and have a dynamic range of at least 20 dB (one hundredfold) without the need to change probes. The readout instrument should be direct reading and free from susceptibility to RF interference.

Many approaches have been used to develop field probes that meet these criteria. The most successful and enduring designs have centered around the thin-film thermocouple or bolometer sensor/antenna and the crystal detector/antenna. The first type of sensor is a square-law-responding device that senses a temperature change due to the absorption of energy. The second type uses a semiconductor diode that produces a voltage or current related to the strength of a field variable. The diode can respond as either a square-law detector or a linear detector, depending on the region in which it is operating. Some commercially available electric-field probes are shown in Figure 3-32.

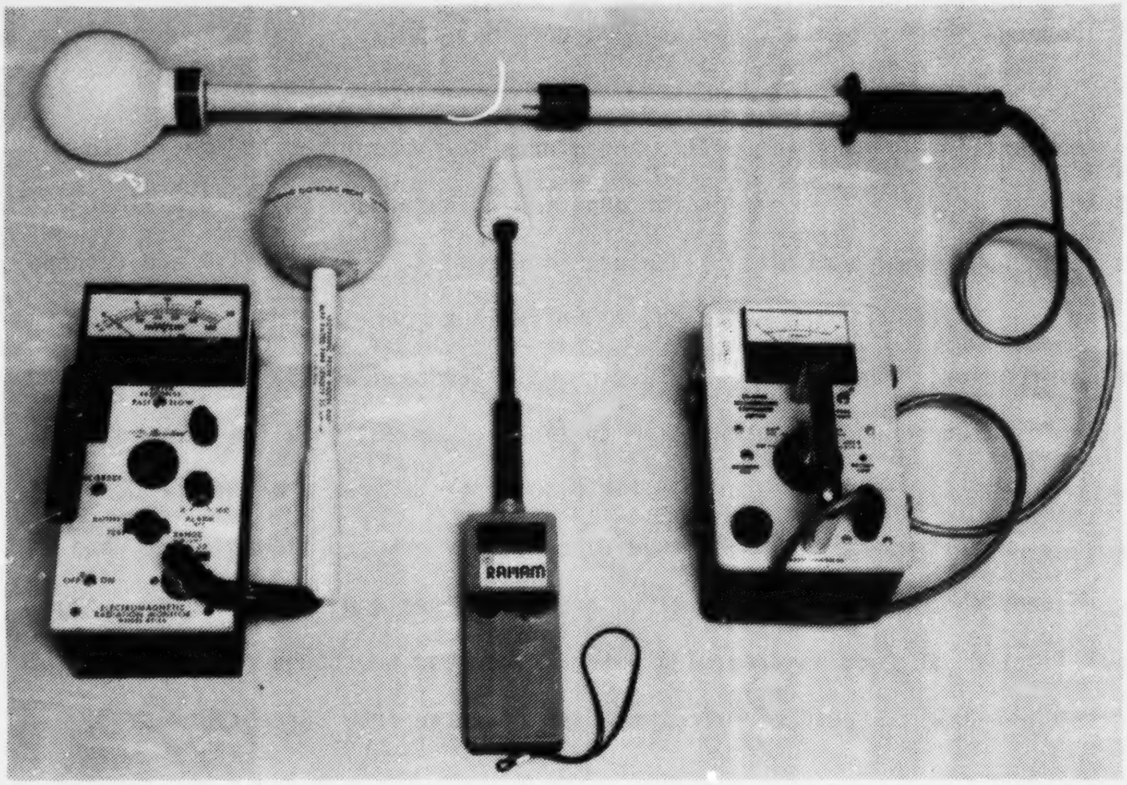


Figure 3-32. Samples of commercially available survey meters for measuring RF electric-field strength. From left to right the units shown are: The Narda Microwave Corporation Model 8315A meter with a Model 8321 isotropic probe; the General Microwave Corporation Model 481A meter with a Model 81 probe; and the Holaday Industries, Inc., Model HI-3001 meter and probe.

3.3.3.1 Electric-Field Probes--

The NBS EDM-2 electric energy density meter (Belsher 1975) was developed for accurate measurement of occupational exposure to EM fields from 10 to

500 MHz. This probe uses three short orthogonal dipoles terminated by crystal rectifiers to detect the RF field, and it produces an isotropic response within ±1 dB. The DC signal appearing on the diodes reaches the meter's electronics through RF-transparent high-resistance lines. The meter displays electric energy density in units of microjoules per cubic meter. Energy density was chosen as the field variable to display because of the ambiguity of power density in the near field of radiating elements.

The meter has a dynamic range of 50 dB in nine ranges from 0.003 to 30 $\mu J/m^3$. Although the probe's detector diodes are used in both the square-law and linear regions, a square-law response is achieved over most of the range by a varistor network. The meter is calibrated at specific frequencies within the FCC ISM bands at 13.56, 27.12, and 40.68 MHz. The frequency response is flat within ±1.0 dB over the 10- to 500-MHz operating range. One of the improvements in the EDM-2 device over previous designs is reduced temperature-induced drift. The reduced drift is achieved by loading the dipole-detector diodes with equivalent load diodes. This technique has reduced the temperature response to $< \pm 0.7$ percent/°C in the 15 to 35 °C range. The field probe design provides a rapid response time to permit observation of the modulation of the field and the measurement of peak values. The rise and fall times (10 to 90 percent of the signal and 90 to 10 percent of the signal, respectively) are both < 0.6 ms on the most sensitive range.

A commercial version of the NBS electric-field probe is marketed by Holaday Industries (Edina, MN). This field-strength meter (Model HI-3001) operates over the frequency range 0.5 to 1000 MHz and is accurate within

±1.0 dB over this range. The meter has an isotropic response within ±1.0 dB and has peak-hold and read circuitry to capture the highest reading observed. The response time is 1.5 s. Measuring range of the meter is 1 to 3160 V/m in six ranges on an analog meter. An audible tone, with a pitch proportional to the meter reading, is provided to prevent operator overexposure in survey applications.

In 1980, the General Microwave Corporation (Farmingdale, NY) introduced the RAHAM Model 4A radiation-hazard meter. This instrument is a broadband crystal-detector design having a frequency coverage of 200 kHz to 26 GHz, and a display calibrated in units of equivalent plane-wave power density ranging from 0.001 to 20 mW/cm^2. This meter has an isotropic response, is battery powered, and has a response time of 1.5 s.

For use in the near field, Rudge (1970) constructed an electric-field probe using two short crossed-dipole antennas. This meter was designed to operate from 915 to 2450 MHz in proximity to RF emitters. The probe detected the electric field in two perpendicular planes, and it was calibrated in power density terms. Rudge carefully analyzed sources of error in the design of near-field probes. His study included the effects of field curvature and antenna backscatter, particularly with regard to multiple coupling and impedance variation, both of which affect the calibration of the field probe. The major source of scattering was the probe's antenna, particularly when the lengths of the dipole wings were on the order of one-fourth wavelength. The prototypal probe achieved a dynamic range of 47 dB with a square-law response. This was accomplished by adding fixed values of load resistances at increasing power levels to keep the detector diode operation in the square-law region.

Sensitivity was reported at 300 nW/cm^2 with a probe antenna of 8-mm overall dipole length.

Bassen _et_ _al_. (1975) developed a miniature broadband probe. Although the probe was designed for free-space operation, the ultimate goal was to develop an implantable isotropic probe for biological effects research (Bassen _et_ _al_. 1977a). Using 3-mm dipole elements, the free-space probe achieved a relatively flat frequency response over the range of 915 MHz to 10 GHz. After some refinements were incorporated (Bassen 1977; Bassen _et_ _al_. 1977b), the probe was tested over a frequency range of 200 MHz to 12 GHz. The improved version had a 30-dB dynamic range with a 20-$\mu W/cm^2$ sensitivity, isotropic response to ±2 dB, a detection bandwidth of 2 kHz, and a spatial resolution of ~ 3 mm.

The requirement of small size was imposed on the implantable-probe design to ensure minimal alteration of the field when the probe is used relatively close to sources and dielectric boundaries. At the same time, the constraint of small dipole size has the further advantage of extending the frequency response of the probe into higher frequencies. With 3-mm dipoles, theoretically, resonance should occur at 50 GHz. The probe uses dipole elements terminated with three zero-bias Schottky diodes for a maximal square-law response, arranged in an "I"-beam configuration. High-impedance leads are connected to the diodes and routed along the probe's body to an optical telemeter. A fiber-optics cable then routes the digitally encoded field-strength signal to a digital receiver that is calibrated to display the equivalent plane-wave power density. A commercial version of the miniature field probe is marketed by Electronic Instrumentation and Technology (Sterling, VA).

An electric-field sensor (EFS) and readout system capable of operating over the frequency range 10 kHz to 200 MHz has been developed by Instruments for Industry, Inc. (Farmingdale, NY) and was described by Ruggera (1976). The EFS-1, -2, and -3 are linearly polarized, square-law electric field detectors with an analog readout calibrated in volts per meter. The EFS-1 is intended for CW fields, the EFS-2 for pulsed fields, and the EFS-3 for both types of fields with the addition of a peak-reading provision. The dynamic range is 1 to 300 V/m with antennas of different lengths. An optical transmitter is used when remote readout is required, eliminating field perturbations introduced by metallic cable. An isotropic monitor has also been designed (RHM series) that essentially encloses three EFS-series sensors in one box. Readings from each sensor can be summed (by the square root of the sum of the squares of the field strengths) to measure the total electric field, or a particular sensor can be read directly when field polarization is a variable of interest.

Another probe design uses thin-film thermocouple arrays acting as both the dipole antenna and the detection element. The dipole elements are lossy; therefore, their temperature will increase proportionally with the square of the tangential electric field. The dipole elements can be thought of as the series connection of a large number of tiny thermocouple dipoles. This detection method provides true square-law response and produces signals proportional to the average energy density of the electric field in the measured volume.

The Narda Microwave Corporation (Plainview, NY) produces a wide selection of RF-radiation monitoring instruments, such as the Model 8606 broadband isotropic radiation monitor. This instrument uses three orthogonal, thin-film thermocouple sensors that respond to the square of the electric field. Two probes are available that have the combined dynamic range of 0.02 to 100 mW/cm^2 over the frequency range 0.3 to 26 GHz. The probes have isotropic response within ±0.5 dB except when the electric field is aligned with the handle axis. The General Microwave RAHAM Model 3, another electric-field-sensitive meter with thin-film thermocouple sensors, performs comparably to the Narda 8606 system. The Narda 8100 series meters were designed earlier (Aslan 1970) for measuring the leakage of microwave ovens, dryers, and medical equipment, which operate at 915 and 2450 MHz. The probe used with the 8100 series meters is not isotropic but must be oriented with the probe handle perpendicular to the wave front. Three probes are used to measure across a dynamic range of 0.02 to 200 mW/cm^2. The probes contain two orthogonal, thin-film vacuum-evaporated thermocouple elements that function both as antennas and detectors. When the probes are used at 915 MHz, an adapter is attached to the end of the probes, increasing the effective length of the dipoles. This increase in length compensates for the reduced efficiency of the antenna at 915 MHz.

3.3.3.2 Magnetic-Field Probes--

As discussed previously, measurement of only the electric field for frequencies below ~ 300 MHz does not fully characterize the hazard or heating potential of an RF field, because the electric and magnetic fields are not related by the free-space intrinsic impedance at frequently encountered distances from radiation sources. In the mid-1970's, NIOSH supported an NBS effort to develop a magnetic field probe that would operate in the 10- to 300-MHz band. Two probes were developed (Greene 1975a,b) that consist of small single-turn, balanced loop antennas of 10- and 3.16-cm diameter. The dynamic ranges of the two probes are 0.5 to 5.0 A/m and 5.0 to 50 A/m, respectively. The probes are capable of measuring the magnetic field within a few centimeters of an RF-radiation source, in the near field. The loop antennas are constructed with two short gaps; one gap is terminated with a silicon diode that detects the induced RF voltage, and the other gap is terminated with a capacitor to bypass RF currents without short-circuiting the DC output. The DC signal is then transmitted over NBS-developed conducting plastic lines to an electrometer voltmeter. One of the inherent problems of loop antennas is that the response is proportional to frequency, making these antennas particularly sensitive to errors if harmonics (integral multiples of the fundamental frequency) are present in the field under study. Greene also shows that both the electric-dipole response of the loop and the partial-resonance effect increase with frequency. An experimental method is provided to minimize the error due to electric-field sensitivity, and plots are provided for the two probes to indicate worst-case measurement error vs. frequency due to the electric-dipole response. The self-resonant frequencies of the two loops were computed to be 280 and 760 MHz for the 10- and 3.16-cm loops, respectively, and a correction curve was provided to estimate the increase in response due to this effect.

Aslan (1976) reported the development of a magnetic-field-radiation monitor that has a frequency response within ±1.0 dB over the frequency range of 10 to 200 MHz. Two probes, the Narda Corporation Models 8631 and 8633, are used to provide a full-scale measurement range of 0.2 to 100 mW/cm^2. (Sensitivity extends to 20 mW/cm^2 on the Model 8631 probe.) These probes have an isotropic response (±0.5 dB) and accept all polarizations. Each probe has three orthogonal coils, with each coil having two turns. The coils are terminated with thin-film thermocouple elements. High-resistance lines are used to route the DC signal to a preamplifier in the handle of the shielded probe, and the preamplifier output is connected via shielded cable to an indicating meter. A partial solution to the problems of frequency dependence of loop antennas was achieved by designing the coils to be series resonant slightly below the low-frequency end of the operating band. The response of the coils increases at frequencies above 200 MHz, as the electric-dipole effect begins to govern the response.

Magnetic-field probes of various designs were reviewed by Ruggera (1976), many of which were commercially available and others of which were experimental. Ruggera described electric-field-shielded loops constructed with semirigid coaxial transmission line from 2 to 6 cm in diameter. Ruggera also described an isotropic, electric-field-shielded, three-loop, orthogonal, magnetic-field probe that has a cross-polarization rejectivity of ~ 20 dB from 40 kHz to 50 MHz. Signals from the probe are recovered with terminated, coaxial cables. In addition, the author described a three-axis, magnetic-field-measuring instrument developed by Southwest Research Institute. The original design was plagued by cable-pickup problems, which limited the usable frequency to 50 MHz. Refinements by the FDA Bureau of Radiological Health

(BRH) that incorporated the optical telemetry systems (see § 3.3.3.1) used on the BRH miniature electric-field probe led to a flatter frequency response over the extended frequency range of 150 kHz to 150 MHz.

In 1981 Holaday Industries introduced a new magnetic-field probe for their 3000 series of field-strength meters. The Model STH-01 probe has a frequency response of 5 to 300 MHz within ±2 dB. The uniformity of response improves to ±1 dB over the range of 10 to 200 MHz. When used with the HI-3001 meter (§3.3.3.1), full-scale sensitivity of the probe is 0.1 A^2/m^2 in the low range and 1.0 A^2/m^2 in the high range. The sensor consists of three orthogonal loops terminated with detector diodes that rectify the RF voltages induced in the loops. The sensors can withstand an 800-percent overload above the full-scale field strength without damage.

3.4 DOSIMETRIC METHODS

James B. Kinn

Dosimetric methods are used to determine where and how much energy is absorbed by a biological target. The methodology is divided into two areas: (1) whole-body dosimetry, dealing with the integrated or spatially averaged SAR for the entire animal; and (2) regional dosimetry, dealing with the SAR's or internal field strengths in a specific site of the biological target.

3.4.1 Whole Body Dosimetry

Whole-body dosimetry is performed using either a power difference or a calorimetric method. The power-difference method is limited to closed exposure systems such as waveguides, TEM-mode transmission cells, and coaxial air lines. In this method, power meters are attached to the exposure systems by directional couplers to measure the incident, reflected, and transmitted power through a section of the closed system containing the biological target. The power absorbed by the biological target is then measured by subtracting the values of the reflected and transmitted power from the incident power. In the case of exposure systems using live animals, the values of those three measurements will vary as the animals move, because absorption is a function of the animal's orientation relative to field polarizations. This makes it desirable to have a data collection system that can integrate the measured power difference and then determine an average over a period of time, usually the exposure duration (Christman _et al_. 1974; Ho and Edwards 1977b). The advantage of this method is that it provides on-line instantaneous measurements of absorbed power. A disadvantage is that its optimum application is in single-animal exposure; simultaneous exposures of multiple animals in the same closed system would result in average dose rate values for the group, rather than for an individual animal. A second disadvantage is that, under exposure conditions where the RF energy absorption rate is very low, it may be impossible to measure the power absorption, because the measurement error in the power meter exceeds the computed power difference.

Calorimetric methods use the thermalization of the absorbed power as a measure of SAR. Under the tacit assumption that all the RF energy absorbed by a biological target is converted to heat, the calorimetric method measures the heat added to the target. The approach is to irradiate an animal carcass with a short exposure at high power to reduce heat loss errors due to conduction and convection during the exposure. The thermalized energy added to the carcass is measured with the calorimeter. Calories per unit time per unit mass are then converted to W/kg, the SAR for this high incident power density. The SAR for any other power density is then scaled from this measured value in direct proportion to the ratio of power densities. Three calorimetric methods that have been used in whole body dosimetry are gradient-layer calorimetry (Gandhi *et al*. 1979), Dewar-flask calorimetry (Blackman and Black 1977), and twin-well calorimetry (Hunt and Phillips 1972; Kinn 1977). All three methods use a freshly killed animal carcass that has been briefly exposed to high-power RF fields and thus raised to a higher temperature. It has been assumed that the dielectric properties of the carcass do not differ significantly from those of a living animal.

The gradient-layer calorimeter measures the rate at which heat passes from the heated animal through the walls of the calorimeter to the room air. It is accurate, but it takes several hours to make the measurement.

The Dewar-flask calorimeter method uses the difference between the average temperature of the animal carcass before and after rapid heating with RF radiation to determine the heating rate and thus the dose rate. The average temperature of the animal carcass is determined by placing the carcass and a coupling fluid, usually water, into a Dewar flask and measuring the equilibrium temperature of the mixture. From the theory of mixtures and a knowledge of the average specific heat capacity of the animal, the average carcass temperature is determined. The average temperature of the heated carcass is determined similarly, and the SAR is computed. Although the method is simple by design, a disadvantage is that a long time is required to measure equilibrium temperature. Furthermore, the average specific heat capacity of the carcass must be known, and, because the body's composition is complex, this capacity cannot be precisely determined.

The twin-well calorimeter method uses pairs of carcasses of equal mass. One carcass of a pair is heated with RF radiation; the heated and unheated carcasses are each placed in a well of the calorimeter, and the calorimeter is allowed to return to equilibrium. The twin-well calorimeter measures the increment of heat introduced by the exposure. The SAR is then calculated from the measured caloric increase, carcass mass, and exposure time. This method does not require the specific heat capacity of the carcass but requires 4 to 16 h to make a measurement. A recent improvement to the method has reduced the measurement time to 15 to 30 min and increased measurement accuracy by controlling the calorimeter with a microprocessor system. This arrangement is the same as the standard setup except that the unexposed carcass is in contact with a heating element (Figure 3-33). The microprocessor program controls the rate at which heat is applied to the unexposed carcass. Using the twin-well calorimeter as a "thermal" balance, the program controls the heating rate so that equilibrium is established in as short a time as possible. All of the power applied to the heating element, and thus to the animal carcass, is integrated and divided by the mass of the carcass to determine the SAR.

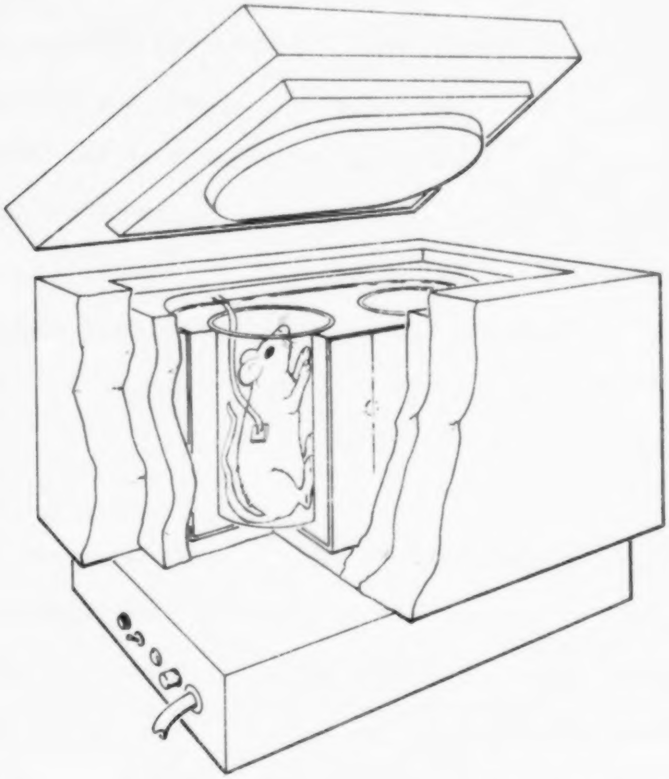


Figure 3-33. Microprocessor-controlled twin-well calorimeter.

3.4.2 Regional Dosimetry

Regional dosimetry is performed to determine either the energy absorption rate or the field strength at a specific location within an animal or tissue preparation. The average field strength within the animal can be measured directly or inferred from the SAR. Direct measurement of field strength is made with an implantable probe containing one or more miniature diodes mounted on a dielectric substrate and attached with high resistance leads to a voltage-reading device (Bassen _et al_. 1977b). The voltage across the diode is a measure of the field strength at the diode, provided the animal tissue material in which the probe is implanted does not differ significantly in dielectric properties from the material used in the calibration procedure (Bassen 1977). The useful frequency range over which such field strength measurements can be made is 100 to 12,000 MHz. The reduced sensitivity at lower frequencies and the greatly reduced field strength in biological targets at the higher frequencies delineate the useful frequency range. Indirect measurement of internal field strength is derived from the SAR value. The heating rate is proportional to the square of the electric-field strength.

Measurement of regional SAR can also be accomplished by temperature probes or by thermographic imaging. Temperature probes are small (1-mm diameter) and are designed to be implanted in the site of interest without altering the EM field in that area (Rozzell _et al_. 1974; Bowman 1976). An animal or preparation is briefly exposed to RF fields of high intensity, and the temperature rise is measured. The rate of temperature rise, together with the amount of heat loss, is then used to compute the SAR at a specific site in an absorber, such as a rat brain.

The technique described above is a special case of heating and cooling curve analysis, i.e., estimating the initial rate when the rate of heating is much higher than the rate of cooling. The analysis of the complete heating and/or cooling curve is especially useful in cases where the RF energy absorption is of the same order of magnitude as the cooling rate of the animal or preparation. In this procedure, the temperature is recorded continuously during exposure and/or after exposure until a steady state or equilibrium temperature is reached. Analysis of either curve yields the cooling rate, which is directly related to the SAR. The heating curve also contains the cooling rate that can be determined by the appropriate analysis; therefore, the SAR can be determined from either a heating or a cooling curve (Allis _et_ _al_. 1977).

Thermographic imaging also requires very high power exposures. This method uses a thermographic camera containing a mirror scanning system, a liquid-nitrogen-cooled detector, and a data collection system usually interfaced to a minicomputer (Guy _et_ _al_. 1977; Kantor and Cetas 1977). Specimens are prepared by cutting a frozen carcass into halves, and supporting each half in an RF-transparent medium such as urethane foam. The surface of the cut plane is covered with either a plastic film or polyester "silk" screen material to hold each half of the specimen in its foam support. The "silk" screen material allows electrical contact between the two halves when they are readjoined during exposure. Unlike plastic film, which prevents induced current from flowing across its surface, the "silk" screen material allows current flow, and the model may be placed in a complex field of unknown polarization. The assembled specimen is allowed to equilibrate to room temperature (25 °C). Thermographic pictures are taken of the animal specimens at the plane of the cut before and after exposure, and the SAR is computed from the point-to-point temperature change during exposure. The SAR values are then used to produce a contour plot of iso-SAR lines or averaged values over a specific area.

Scaled-down or full-size phantoms made with materials having dielectric properties similar to those of biological tissues are also used to determine the SAR distribution in a biological specimen, such as man and small animals. Animal models have been used for the investigator's convenience. Scaled models of man (Guy *et al*. 1976; Gandhi *et al*. 1977) have been used to simulate human exposures under varying conditions. This involves frequency scaling, in which a combination of higher-frequency radiation with a smaller-than-life-size model is used to simulate the absorption characteristics of man when exposed to lower-frequency radiation. The technique also requires suitable scaling for the dielectric parameters of the tissue-equivalent materials used in the model. The validity of the models used to date is open to some question, because the phantom "equivalent" model is filled with a homogeneous material whose complex dielectric constant is the estimated average for the whole body; a more realistic model would attempt to simulate the inhomogeneous tissue structure of the body. The dielectric material normally used in human modeling is gelled water whose conductivity has been adjusted with sodium or potassium chloride. The phantom is made in two halves, and the thermographic method described above for animal specimens is used.

3.4.3 Unresolved Questions

Refinements are lacking for models of the inhomogeneous tissue structure of man and animals, and the equivalency of these models to the actual biological target has not been validated. In simultaneous exposure of multiple animals, to what extent do animal movements create uncertainty in the SAR estimates? How much target separation is required before this uncertainty falls within acceptable limits? As the sophistication of research into RF-induced biological effects improves, and as the sites for many of the reported effects--particularly those associated with the nervous system--become better isolated and defined, there will be an ever increasing need for localized dosimetry of greatly improved spatial resolution. Finally, although it is well understood that RF energy is converted to heat in a biological target, the question remains: Are there transient "field-specific" effects not explicable by a temperature change?

SECTION 4

EFFECT OF RF-RADIATION EXPOSURE ON BODY TEMPERATURE

4.1 THERMAL PHYSIOLOGY

Christopher J. Gordon

4.1.1 Temperature Regulation

Almost all animal species, including vertebrates and invertebrates, are capable of sensing and responding to changes in environmental temperature. The ability to maintain a constant body temperature independent of ambient temperature, termed homeothermy, is restricted to humans and other mammals as well as most birds. Reptiles, amphibians, fish, and invertebrates generally have a body temperature similar to ambient temperature, and are thus termed poikilotherms (i.e., having changeable temperature).

Below the point of protein denaturation, temperature has a direct effect on the rate of biochemical reactions and thus affects the rate of physiologic processes. The effect of temperature on biological reactions is described by the Q_{10} parameter, a dimensionless number equal to the increment in the reaction rate for a 10 °C increase in temperature:

$$Q_{10} = \left(\frac{R_2}{R_1}\right)^{10/T_2 - T_1}$$

or

$$\log Q_{10} = (10/T_2 - T_1)(\log R_2 - \log R_1)$$

where R_1 = reaction rate at T_1

R_2 = reaction rate at T_2

T = temperature

Thus, a Q_{10} of 2 means that the reaction rate doubles with a 10 °C increase in temperature, a Q_{10} of 3 means a tripling of the rate, and so forth. For biological reactions, the Q_{10} generally ranges between 2 and 3.

The activity of poikilotherms is dictated by environmental temperatures. At low temperatures enzymatic activity is decreased, causing reduced muscle activity, active transport, etc. Hence, poikilotherms generally have a narrow range of ambient temperatures (~ 20 to 40 °C) where normal life functions can take place. On the other hand, many homeotherms, by maintaining a relatively constant body temperature, can function normally at ambient temperatures far below 20 °C and occasionally above 40 °C. Of course, to maintain a constant body temperature at extremely high and low ambient temperatures requires additional metabolic energy.

There are three major physiologic systems employed by homeotherms when subjected to changes in ambient temperature: (1) the neurally activated behavioral and autonomic motor systems, (2) the neurally activated hypothalamohypophyseal system, and (3) the morphology and growth system. The following is a brief explanation of each physiological system. (1) During a thermal stress, thermal receptors in the skin, central nervous system (CNS), and other deep body areas are activated. The neural activity is integrated predominantly in the preoptic area and anterior hypothalamic area of the brain stem where the proper motor signal originates to either generate or dissipate heat (Figure 4-1). Cold-exposure may result in vasoconstriction of peripheral blood vessels, shivering, and selection of a warmer environment. Heat exposure may result in vasodilation of peripheral blood vessels, sweating or panting, and selection of a cooler environment. (2) If the thermal stress continues for at least several minutes, the CNS responds by changing blood hormone levels. In both heat and cold stress there is an increased release of adrenocorticotropin from the pituitary, which in turn increases blood corticosteroids. Cold stress facilitates the increased secretion of thyroxine from the thyroid gland and epinephrine from the adrenal medulla. Heat stress facilitates the release of vasopressin, the water-conserving hormone. (3) Prolonged thermal stress for weeks and months will promote morphologic changes designed to reduce the impact of the thermal stress. For example, raising animals in cold environments will result in shorter appendages, increased fur density, and cutaneous fat deposition, which reduces the rate of heat loss.

4.1.2 Ambient Temperature vs. RF-Radiation Exposure

The physical mechanisms underlying the regulation of a constant body temperature during normal temperature or RF-radiation exposure can be described

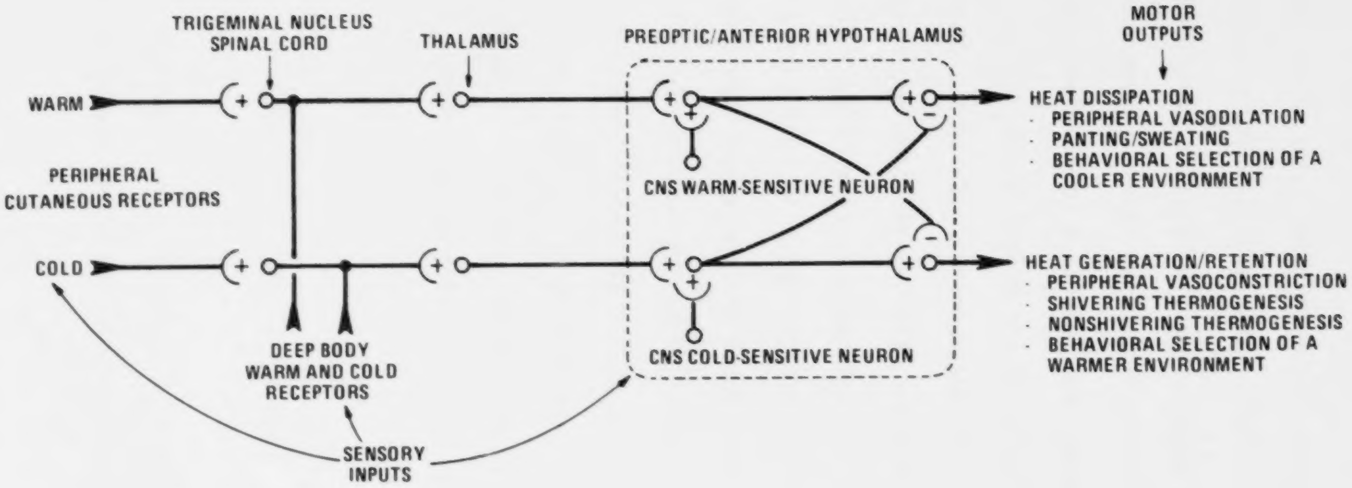

TRIGEMINAL NUCLEUS
SPINAL CORD
THALAMUS
PREOPTIC/ANTERIOR HYPOTHALAMUS
MOTOR
OUTPUTS
WARM
+
+
+
+
+
-
HEAT DISSIPATION
· PERIPHERAL VASODILATION
· PANTING/SWEATING
· BEHAVIORAL SELECTION OF A
COOLER ENVIRONMENT
PERIPHERAL
CUTANEOUS RECEPTORS
CNS WARM-SENSITIVE NEURON
COLD
+
+
+
+
+
-
HEAT GENERATION/RETENTION
· PERIPHERAL VASOCONSTRICTION
· SHIVERING THERMOGENESIS
· NONSHIVERING THERMOGENESIS
· BEHAVIORAL SELECTION OF A
WARMER ENVIRONMENT
DEEP BODY
WARM AND COLD
RECEPTORS
CNS COLD-SENSITIVE NEURON
SENSORY
INPUTS

Figure 4-1. Simple neural model of thermoregulation in a mammal for predicting the motor responses to short-term (i.e., hourly) changes in ambient and/or body temperature. Activation of the warm-sensitive pathway leads to an increase in heat dissipatory mechanisms, whereas activation of the cold-sensitive pathway leads to an increase in heat generating/retaining mechanisms. This information is taken from several models proposed by Hammel (1968) and Hensel (1973).

using a simple model (Figure 4-2). Under steady-state thermoneutral conditions, the direction of heat transfer is from the inner core (e.g., core or rectal temperature, T_c) to the cooler peripheral shell (e.g., skin and subcutaneous temperature, T_{sk}). In the absence of blood flow the transfer of heat between the core and periphery is approximately equal to the intershell temperature gradient multiplied by the heat conductivity of the tissues. Heat exchange between the skin and environment occurs through convection, radiation, and evaporation. Under most conditions the transfer of heat within the central and peripheral shells is greatly influenced by the circulation of blood. Raising the temperature of either the peripheral or ambient shell impedes the transfer of heat and results in an increase in T_c.

Either an elevation in ambient temperature or exposure to RF radiation may lead to an increase in body temperature; however, the route of heat transfer from the two heat sources varies greatly. For example, raising ambient temperature reduces the temperature gradient between T_{sk} and T_a, resulting in an elevated T_{sk}. The higher peripheral shell temperature, which in turn reduces the T_c-T_{sk} gradient, causes an increase in T_c. In contrast, RF-radiation exposure can increase the temperature of the T_c and T_{sk} without affecting T_a by direct deposition of energy in the peripheral and/or core shells.

4.1.3 Mechanisms of Heat Gain During RF-Radiation Exposure

The coupling of electromagnetic (EM) energy into biologic subjects exposed to RF radiation was discussed in detail in § 3.2, RF-Field Interactions with

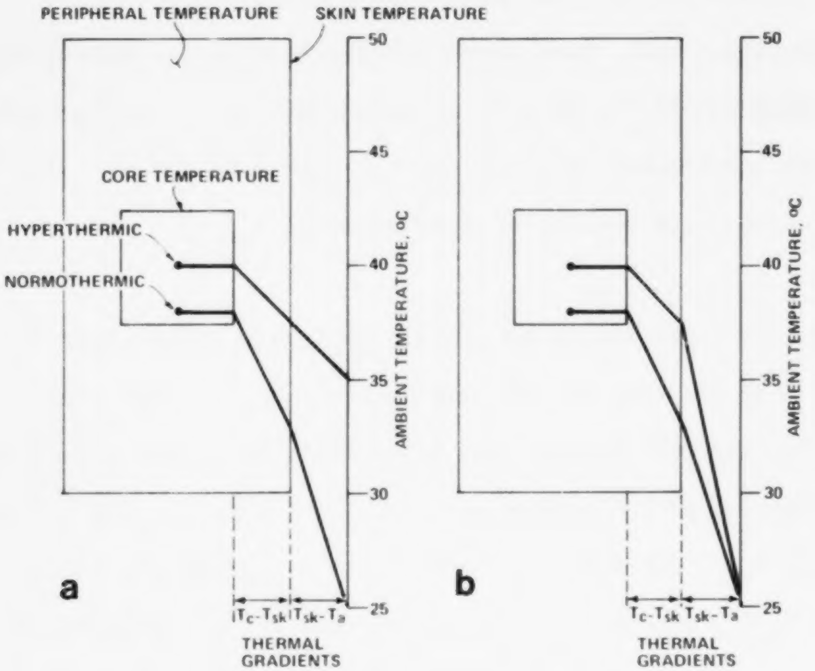

PERIPHERAL TEMPERATURE
SKIN TEMPERATURE
CORE TEMPERATURE
HYPERTHERMIC
NORMOTHERMIC
a
b
50
45
40
35
30
25
AMBIENT TEMPERATURE, °C
T_c-T_{sk}
T_{sk}-T_a
THERMAL GRADIENTS

Figure 4-2. Simple model of temperature gradients in a homeotherm under conditions of thermal neutrality, normal heat stress (a), and heat stress due to RF-radiation exposure (b). At a thermoneutral ambient temperature, the skin temperature T_{sk} is maintained at approximately 33 °C. (a) Raising ambient temperature to 35 °C results in an elevated T_{sk}, which in turn causes an increase in core temperature T_c. (b) Exposure to RF radiation causes an elevation in the peripheral temperature without affecting T_a and promotes an elevated T_c.

Biological Systems. To introduce the following material, some of the important features of that discussion will be reiterated and summarized here.

The penetration of RF energy into biological tissues is dependent on the wavelength of the incident energy. Longer wavelengths can penetrate deeply into living tissues, but the shorter wavelengths found in the microwave region of the spectrum cannot penetrate deeply. For example, at 2450 MHz (wavelength of 12.5 cm) the RF energy is absorbed within approximately the first 4 to 5 cm of muscle tissue, assuming that the RF radiation is incident on an object that is large in comparison to this wavelength (such as a human). Similarly, RF energy of still higher frequencies (i.e., in the millimeter wave region of the RF spectrum) will not penetrate more than 1 to 2 mm in skin tissue.

This difference in penetration poses a major problem for comparing the effects of RF radiation of very different wavelengths on thermoregulatory function in different species. For example, when a 20-g mouse or a 70-kg man is exposed to RF radiation of millimeter-size wavelengths or to infrared (IR) radiation, the energy is deposited in the first 1 to 2 mm of the skin in a basically similar fashion. However, at 2450 MHz a mouse is comparable in size to the wavelength so that a resonant absorption condition exists, resulting in efficient energy coupling with deep penetration and nonuniform internal energy deposition (i.e., EM radiation "hot spot" formation). On the other hand, when a human is exposed to the same 2450-MHz radiation, the energy will be peripherally deposited within a few centimeters of the body's surface in that area facing the radiation source.

Notwithstanding these problems, some attempts have been made to compare thermoregulatory function in different species when subjected to RF radiation of the same frequency. For example, deLorge (1979) compared the power density at 2450 MHz needed to induce a 1 °C elevation in the rectal temperature of rats, squirrel monkeys, and rhesus monkeys. Using a semi-log plot of power density vs. body weight (Figure 4-3), deLorge extrapolated the data on rats and subhuman primates to the case of a 70-kg man. He determined that a value of 92 mW/cm^2 is needed to raise the rectal temperature of man by 1 °C at

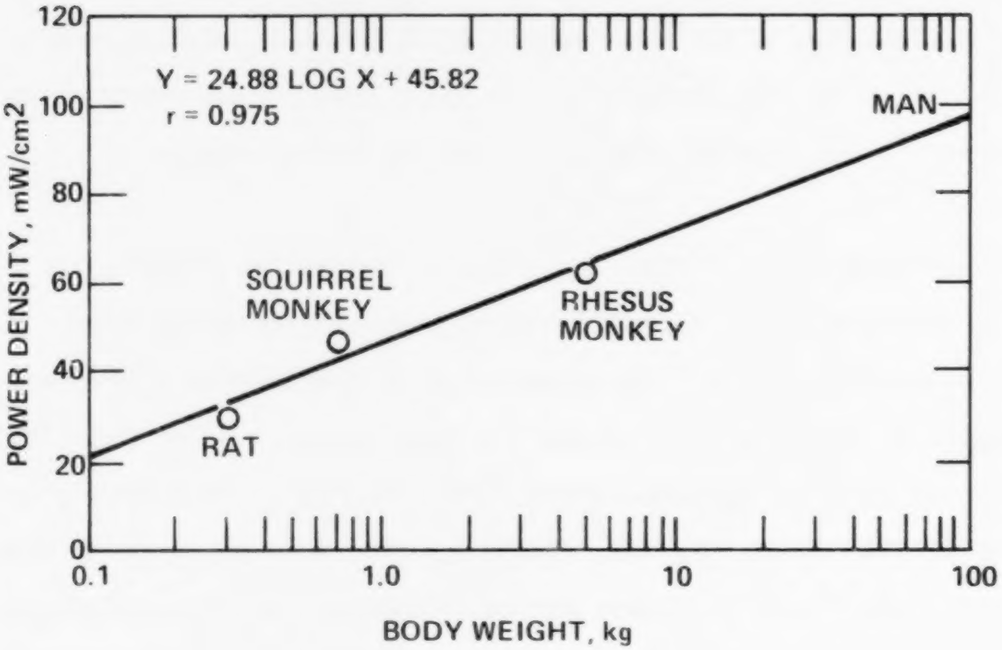


Figure 4-3. Power densities at 2450 MHz necessary to raise the rectal temperature by 1 °C in 60 min for the rat, squirrel monkey, and rhesus monkey (deLorge 1979).

2450 MHz. This comparison is probably acceptable because, for the four species considered, a supraresonant kind of EM interaction takes place at this frequency (see § 3.2). This means that the coupling of RF energy into the animal is less than optimal (i.e., the coupling is of intermediate efficiency), and most of the energy is peripherally deposited, although less so for the rat than for the man. If the same interspecies comparison were to be performed under conditions in which the RF-radiation coupling is optimal (i.e., the resonant absorption case), then the results will likely be very different (i.e., the power density values needed for a 1 °C elevation in rectal temperature may well be significantly reduced by a factor of 8 or more). Tell and Harlen (1979) have also pointed out that if a human were exposed to 2450 MHz at a power density of approximately 90 mW/cm^2, irreversible local peripheral tissue damage will likely result without any change in rectal temperature.

When there are supraresonant-type interactions, the absorption coefficient is roughly constant and is ~ 0.5. Under these conditions, the RF-energy absorption depends only on the geometric cross-sectional area of the exposed animal. Assuming a spherical shape of radius r for the animal, it can be shown that the cross-sectional area-to-volume ratio is proportional to $r^{2/3}$ (Kleiber 1961). This means that the area-to-volume ratio as well as the area-to-mass ratio will decrease as the animal increases in size. Consequently, the absorbed energy per unit of body mass (i.e., whole-body-averaged specific absorption rate, SAR) decreases with increasing size. This general rule of thumb is valid only for interaction conditions of the supraresonant type, and it is not valid for resonant- and subresonant-type conditions.

SAR at 2450 MHz as a function of body weight with the body axis aligned with the electric field is shown in Figure 4-4. By taking the threshold power density for a 1 °C rise in temperature (Figure 4-3) and converting to SAR, it is predicted that an inverse relationship exists between body weight and SAR to evoke a 1 °C rise in temperature. For example, a power density of 33 mW/cm^2 for a 0.3-kg rat translates to an SAR of 7.9 W/kg; whereas, for a 70-kg man, a power density to evoke the same 1 °C rise in temperature, 92 mW/cm^2, translates to an SAR of 2.1 W/kg.

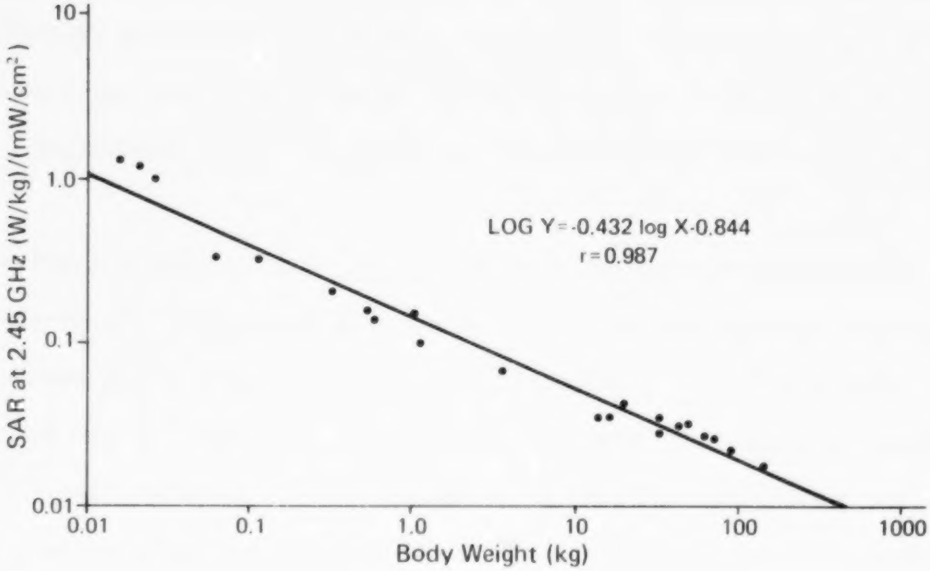


Figure 4.4 SAR as a function of body weight.

4.1.4 Local Thermal Responses: Effect of RF-Radiation Exposure on Blood Flow

Interest during the early 1940's in using short-wave diathermy (13 to 43 MHz) as a therapeutic agent prompted research into the effect of RF radiation in producing localized changes in peripheral blood flow. Near-field diathermic application with capacitance plates (SAR not determined) was shown to produce a more than twofold increase in blood flow of an exposed limb of a dog (Wakim et al. 1948) and of a human (Abramson et al. 1957). Using the ^{133}Xe clearance technique, McNiven and Wyner (1976) found that localized exposure to 2450 MHz caused a nearly fourfold increase in blood flow of the *vastis lateralis* muscle in humans. Although it was not possible to determine the SAR, this study is important because it contains some of the few data collected concerning RF effects on blood flow in humans.

RF-radiation-induced increases in peripheral blood flow can be attributed to a direct effect of heat on the caliber of arterioles, or to an indirect, neurally induced, vasodilation via the activation of peripheral and deep-body thermal receptors. The increase in femoral blood flow during RF-radiation exposure (2450 MHz and 27.3 MHz) is similar in dogs with intact and denervated limbs (Siems et al. 1948). Hence, RF radiation can directly affect peripheral vascular resistance; however, the fact that this response occurs in the denervated limb does not preclude a neural response to RF radiation under normal circumstances.

Adair and Adams (1980a) found that RF-radiation exposure of the squirrel monkey to 2450 MHz at 8 to 10 mW/cm^2 (SAR=1.5 W/kg) promoted vasodilation in the tail and foot without any change in rectal temperature. Furthermore, it was shown that an equivalent power density of IR heat, which has a much shorter wavelength and is absorbed on the skin surface, was ineffective in promoting vasodilation. Exposing the squirrel monkey to RF radiation promotes vasomotor responses similar to direct heating of the preoptic anterior hypothalamus, an extremely thermal-sensitive area of the brainstem considered an integrative center for the control of body temperature. Hence, it was concluded that RF-induced vasodilation was caused by the activation of warmth-sensitive neural sites in and/or outside the CNS, which in turn affect the central neural control of heat-dissipating motor outputs, including the dilation of the peripheral vasculature.

4.1.5 Whole-Body Thermal Response to RF-Radiation Exposure and Dependence on Ambient Conditions

Figure 4-5 displays an idealistic metabolic response of a homeotherm to changes in ambient temperature. The range of ambient temperature where metabolic rate remains at a stable and minimal level is defined as the thermoneutral zone. As ambient temperature decreases in the thermoneutral range, the rate of heat loss increases, and the homeotherm responds with an increased peripheral vasoconstriction. If ambient temperature decreases to a point where the animal's physical mechanisms for restricting heat flow are maximized, then metabolic heat production (mostly from shivering) is elevated to match the heat loss. The upper critical temperature defines the upper limit of the thermoneutral zone where metabolism starts to rise with increasing ambient temperature. Heat stress increases metabolism directly by raising the

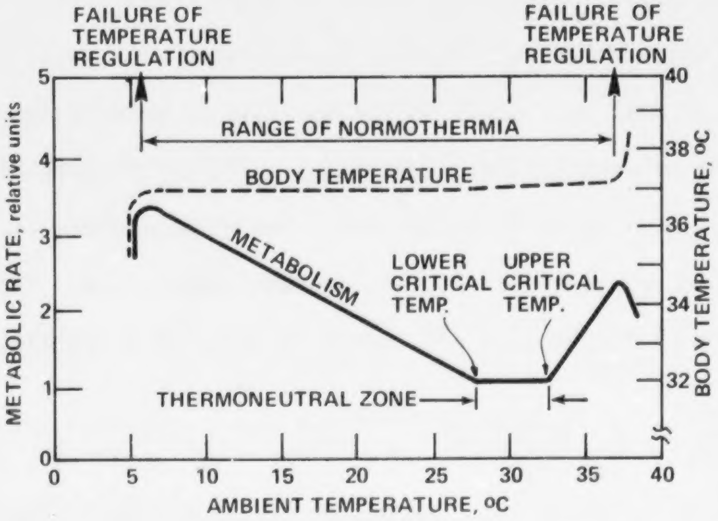


Figure 4-5. Idealistic response of a homeotherm's metabolism and body temperature to changes in ambient temperature. The upper and lower critical temperatures greatly depend on the animal's size and adaptability to warm or cold environments. When the limits of normothermia are exceeded, death from hypo- or hyperthermia is imminent.

temperature of peripheral tissue. A 10 °C increase in tissue temperature results in an approximate doubling of the oxygen consumption rate. (See discussion above.) Heat stress also raises the oxygen requirement by evoking an increase in ventilation. Upper and lower critical temperature and profile of metabolism (i.e., shape) vary tremendously with species.

When a homeotherm is exposed to a thermal stress, whether it be an elevated ambient temperature or an RF-radiation exposure, if the heat gain from the environment plus basal metabolic heat exceeds the animal's capacity for heat dissipation, there will be an increase in body temperature.

Above the lower critical temperature, homeotherms rely on evaporative water loss (EWL) to dissipate excess heat. A major route of EWL is the respiratory passages where relatively dry air is saturated with water and exhaled with the amount of heat loss equal to the quantity of water evaporated multiplied by the heat of vaporization (580 cal/g). The major route of EWL in humans is sweat vaporization from the skin. The effectiveness of this mechanism depends upon relative humidity and ambient temperature. Increasing the relative humidity of the ambient air lowers the rate of evaporization.

Since a homeotherm's metabolic rate is dependent on ambient temperature, the response to RF radiation also depends on environmental temperature. For example, in mice held at 24 °C (lower critical temperature = 29 to 30 °C), exposure to 2450 MHz at 20 to 30 W/kg results in a depression in metabolic rate (Ho and Edwards 1977a). Apparently, when metabolic rate is elevated above basal conditions during cold exposure, the heat absorbed during RF-radiation exposure can be substituted for metabolic heat, and therefore results in a lowering of metabolism.

The pre-exposure heat balance of the animal should be considered when measuring thermoregulatory responses to RF radiation. Ho and McManaway (1977) used direct calorimetry to measure the heat dissipation of mice before and after 30 min of exposure to 2450 MHz at 24 °C ambient temperature. The mice could absorb from 0 to 25 W/kg with no detectable rise in heat dissipation. Above 25 W/kg there was a clear increase in the rate of heat loss. At 20 °C ambient temperature, evaporative heat loss (EHL) in mice is stable between SAR's of 0 and 29 W/kg. Above 29 W/kg, EHL increases with SAR with a slope of

0.6 (i.e., above threshold, 60 percent of the absorbed RF-heat load is dissipated by evaporation; Figure 4-6a). It is expected that the threshold for EHL activation is reduced at higher temperatures. For example, various exposure durations of 2450 MHz at 49 W/kg elevate EHL but only after a distinct threshold is exceeded. Furthermore, the percent of the heat load dissipated by evaporation increases with ambient temperature (Figure 4-6b).

When a homeotherm is pushed into a positive heat balance (e.g., heat gain from metabolism and environment exceeds heat loss) during RF-radiation exposure, there are three distinct phases that describe the change in deep-body temperature. Michaelson *et al*. (1961) exposed unanesthetized dogs to 2800-MHz pulsed-wave (PW) radiation at 100 to 165 mW/cm^2 while recording changes in rectal temperature. During the first 25 min of exposure, there is a 1 °C increase in deep-body temperature, followed by a stabilized period of hyperthermia lasting 30 to 40 min. A similar body-temperature rise followed by a stabilization period has been observed in the rhesus monkey (Krupp 1977). If exposure continues, the mechanisms of heat dissipation apparently become exhausted, and body temperature rises to dangerously high levels. Sustained body temperatures of 42 to 45 °C are considered lethal. The maintenance of adequate body-water levels is critical in regulating stable body temperature during prolonged RF-radiation exposure. The body temperature of dehydrated animals will increase much more than that of hydrated ones during such exposure (Michaelson *et al*. 1961).

In addition to ambient temperature and body-water levels, the relative humidity is another critical determinant of an animal's body-temperature

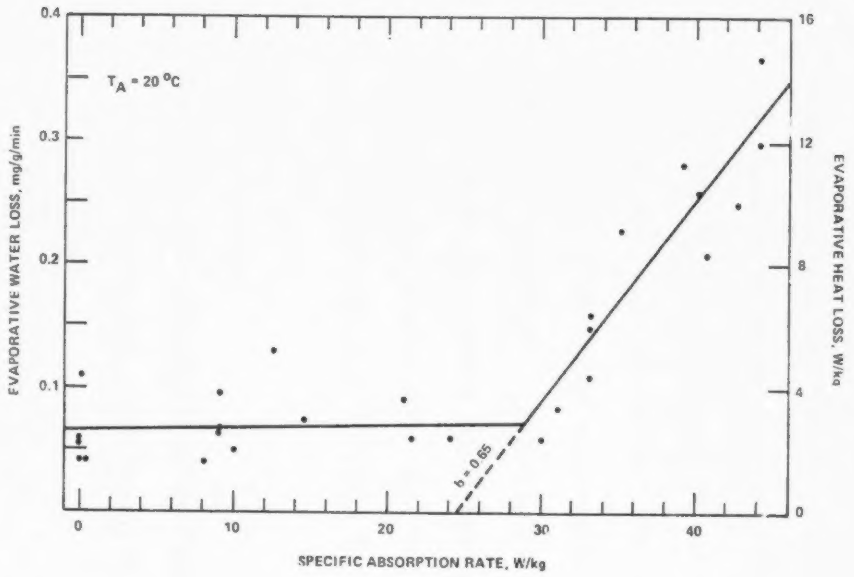


Figure 4-6a. Relationship between SAR at 2450 MHz and EHL in male mice maintained at 20 °C ambient temperature (Gordon 1982a).

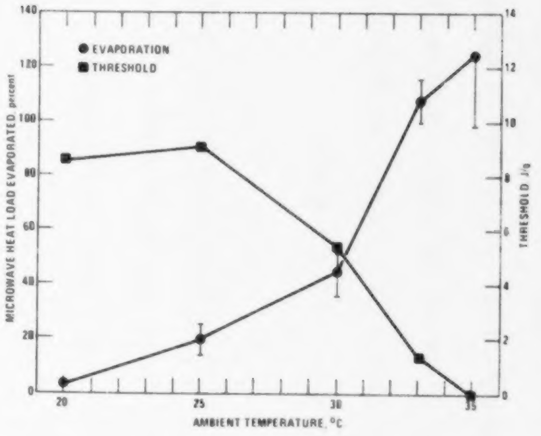


Figure 4-6b. Effect of ambient temperature on the sensitivity of EHL in mice exposed to various RF heat loads at 2450 MHz. Note that threshold is inversely related, and the sensitivity (percent heat evaporated) is directly related to ambient temperature.

response to RF-radiation exposure. A temperature-humidity index (THI) has been developed that defines ambient conditions important to heat balance during RF-radiation exposure (Mumford 1969; Rugh _et al_. 1974). The THI is calculated from the following equation:

$$\mathrm{THI} = 1.41T + 0.1RH + 30.6$$

where T = ambient temperature (°C)

RH = relative humidity (percent)

Using THI's between 50 and 95, Rugh _et al_. (1973) found that the average lethal dose (J/g) for male mice decreased linearly with an increasing THI (Figure 4-7). Raising the THI decreases the rate of heat loss in two ways: (1) The body temperature-ambient temperature gradient is reduced, decreasing the rate of heat loss by convection and radiation; and (2) the elevated relative humidity reduces the vaporization of water from the respiratory passages. Hence, the animal's net heat balance increases with increasing THI, thereby reducing the lethal dose for RF-radiation exposure.

4.1.6 Heat Stress and the General Adaptation Syndrome

Since the majority of biological effects from exposure to RF radiation can be attributed directly or indirectly to tissue heating, a brief discussion on the health effects of heat stress is necessary. Exposing a mammal to heat stress, either by elevating ambient temperature or by local heating of the hypothalamus (Gale 1973), leads to an activation of the hypothalamic-pituitary-adrenal-cortex axis with a resulting elevation in blood glucocorticoids. This

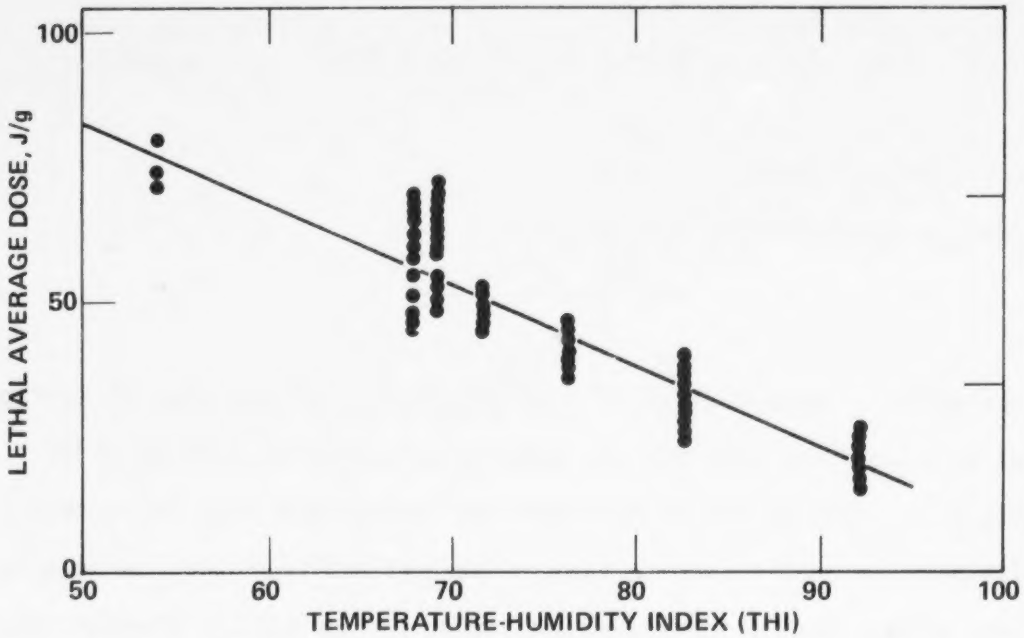


Figure 4-7. Effect of an increasing THI on the lethal dose of RF radiation (2450 MHz) in mice (Rugh _et al_. 1973).

response is part of a series of physiological events known as the General Adaptation Syndrome, since it occurs with non-heat-related stress as well. Increased glucocorticoids (e.g., cortisol and cortisone) in the blood can promote an array of physiological and pathophysiological changes (Harper 1975) such as those listed:

- Elevation in blood levels of glucose, fatty acids, and amino acids
- Reduction in muscle protein synthesis
- Reduction in the inflammatory response
- Suppression of immune system
- Increased gastric acidity
- Osteoporosis (weakening of bones)
- Elevated blood pressure

Not all of these physiological changes have been shown to occur with heat stress; however, any one of the above symptoms could be manifested, since heat stress can evoke release of the glucocorticoids.

4.1.7 Thermal Physiology of Humans

In view of the paucity of studies on human physiology during RF-radiation exposure, this report has centered primarily on the responses of laboratory mammals. One must be cautious in relating measured biological effects in experimental mammals to man, however, because the thermal physiology of humans and other mammals may differ substantially. The following discussion briefly summarizes the major physiological responses of humans to heat stress.

A major difference between humans and most experimental mammals is the ability to secrete sweat on the skin. Under resting, thermoneutral conditions there is a certain amount of insensible EWL through the skin, which accounts for about 8 W of heat. Approximately 25 percent of the total metabolic heat is lost through evaporation at rest. With thermal stimulation the amount of heat lost by evaporation increases tremendously. The partitioning of heat loss at various ambient temperatures in humans is listed in Table 4-1.

TABLE 4-1. PARTITIONING OF HEAT LOSS IN HUMANS AS A FUNCTION OF AMBIENT TEMPERATURE*

Ambient Temperature (°C)	IR (%)	Convection (%)	Evaporation (%)
25	67	10	23
30	41	33	26
35	4	6	90

*Folk 1974.

Sweating from the skin of man and other primates can be evoked by heating the skin or thermally sensitive sites in the nervous system (Figure 4-8a). It is interesting to compare the relatively high threshold of sweating at low vs. high skin temperatures (Figure 4-8b). This comparison may be relevant to some frequencies of RF radiation that heat predominantly the inner tissues and organs without warming the skin. Such latencies may affect the organism's ability to respond to RF heating.

It is important to understand the thermoregulatory responses of humans during exercise, since it represents one of the few cases where internal temperature can increase without rising ambient temperature and, in this respect, is similar to that of RF heating. Humans are well adapted to dissipate excess heat loads from exercise. Examples of thermoregulatory responses during two

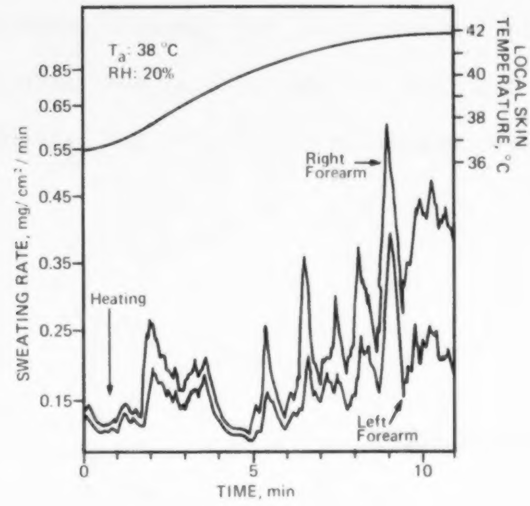


Figure 4-8a. Effect of increasing skin temperature on sweating from the forearms of a human (Elizondo 1973).

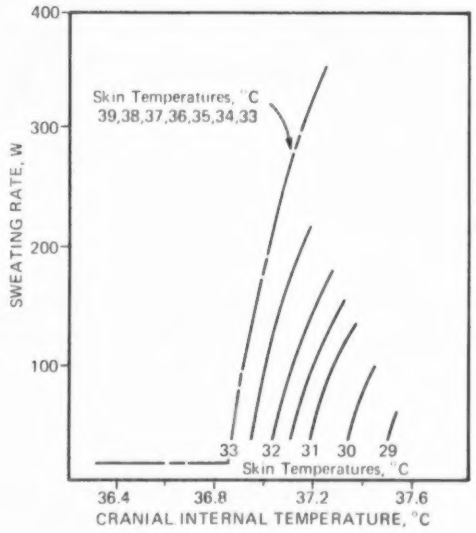


Figure 4-8b. Effect of skin temperature on the threshold internal cranial temperature for activation of sweating in humans (Benzinger 1969).

levels of exercise are shown in Figure 4-9. A work load of 40 W causes an increase in metabolism from 1.5 to 4.2 W/kg and a concomitant 0.34 °C rise in tympanic temperature; the temperature of the tympanic membrane in the ear is considered to be a good indicator of the internal temperature of the head. A 90-W work load increased metabolism to 7.0 W/kg and raised tympanic temperature by 0.96 °C.

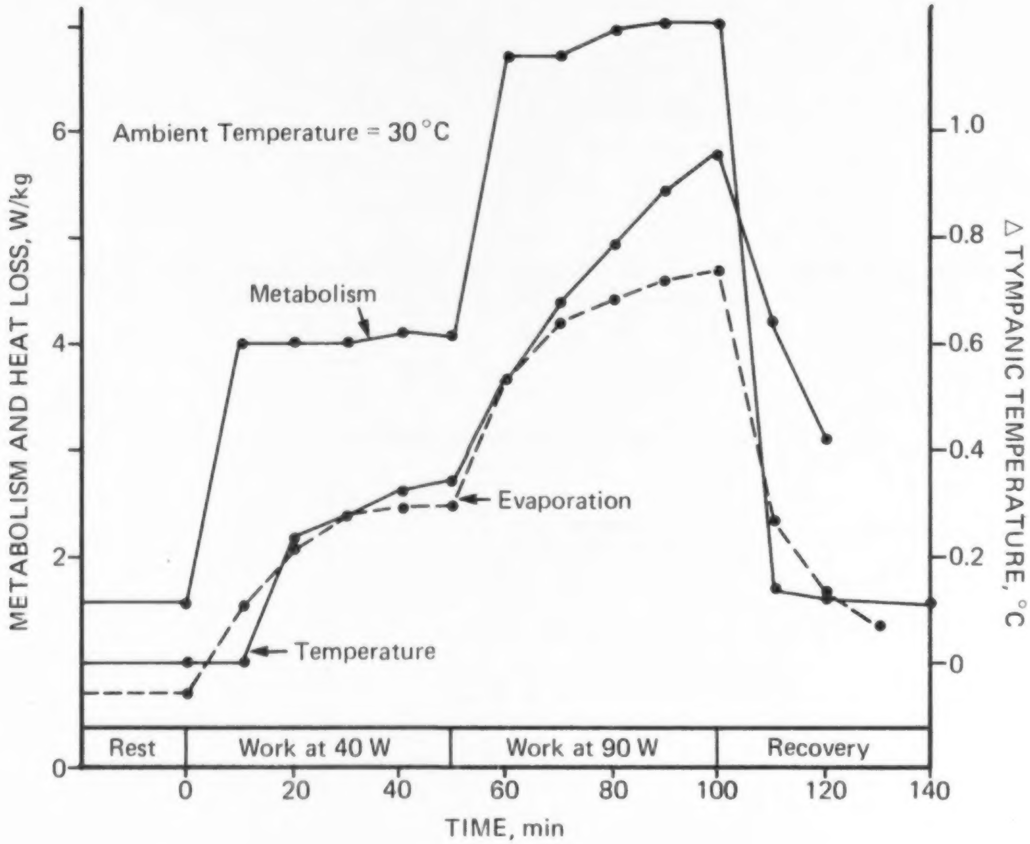


Figure 4-9. Effect of exercise on heat loss, metabolic rate, and tympanic temperature of humans (Chappuis *et al*. 1976).

It is interesting that the rise in metabolism from peddling the ergometer and the heat load normalized to time and weight from RF-radiation exposure have the same dimensions (W/kg). Of course, the two forms of heat cannot be considered to evoke the same physiologic effects. However, measuring the rise in body temperature, evaporation, and other physiological parameters during an exercise-induced heat load may aid our understanding of human response to RF radiation. It is clear from the data in Figure 4-9 that healthy humans can tolerate metabolic heat loads of 7.0 W/kg without significantly stressing the thermoregulatory system. However, it remains to be shown if, under similar circumstances, humans can tolerate RF- heat loads of the same magnitude.

There are numerous reports on the effects of chronic and acute heat stress on man. A few of the symptoms that occur with extreme heat stress (Folk 1974) are listed below:

- Initial increase in plasma volume as fluid shifts from the interstitial spaces into the vasculature. Several days of heating increases the number of red blood cells. Hence, blood viscosity can be elevated, which in turn increases the work load on the heart.
- Initial exposure to heat results in a transient hypoglycemia.
- Food consumption is initially elevated, but anorexia is associated with prolonged heating. Spontaneous activity is also reduced with heat stress.
- As the heat stress progresses, dehydration will occur along with an elevation in body temperature.
- Pulse rate is increased.
- Urine volumes are reduced, and the urine is more concentrated.

Ellis _et_ _al_. (1960) have provided the following criteria for the termination of heat exposure in humans during intermittent periods of work:

- A pulse rate of 160 beats/min after working in the heat
- A pulse rate of 140 beats/min before starting work
- A rectal temperature of 39.2 °C or higher
- A rising pulse rate during the rest period
- Complaints of unpleasant symptoms (e.g., cramps or faintness)

4.1.8 Thermoregulatory State and Physiological Responsiveness to RF Radiation

A recent investigation by Smialowicz _et_ _al_. (1982) has employed a unique form of cold stress as an assay for detecting the physiologic effects of low level RF-radiation exposure. Smialowicz _et_ _al_. found that mice injected intraperitoneally with 5-hydroxytryptamine (5-HT) became hypothermic, the decrease in body temperature being inversely related to ambient temperature (Figure 4-10). The 5-HT-induced hypothermia is attenuated in a dose-related response by exposure to 2450-MHz radiation at 1 to 10 mW/cm^2 (Figure 4-10). The linear regression of colonic temperature after 5-HT vs. ambient temperature calculates to a slope of 0.30 °C colonic temperature/°C ambient temperature. Plotting the 5-HT hypothermia against RF-radiation power density calculates to a slope of 0.15 °C colonic temperature/1.0 mW/cm^2. Dividing the ambient temperature response by the RF-radiation response we obtain:

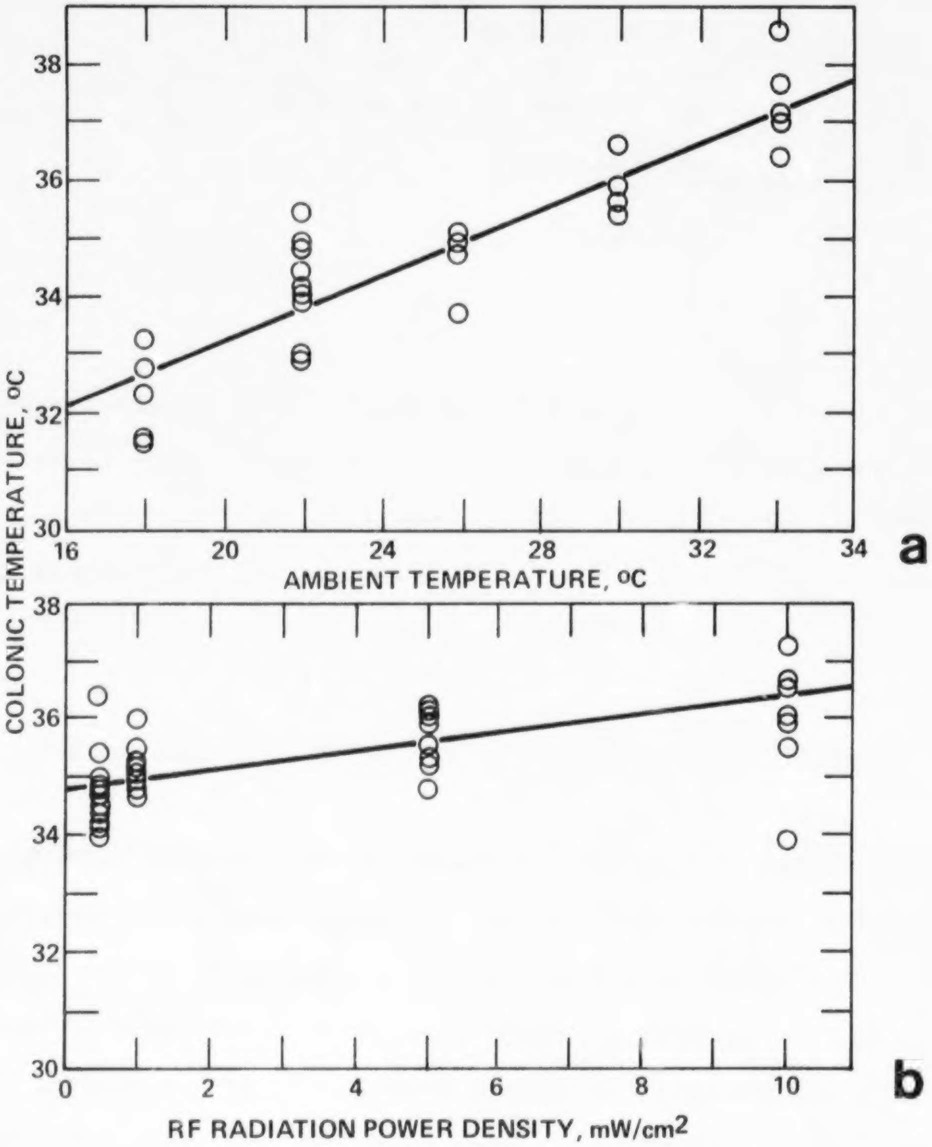


Figure 4-10. Effects of 5-HT injections on mice (Smialowicz *et al*. 1980a).

(a) Linear regression of colonic temperature after an intraperitoneal injection of 5-HT at various ambient temperatures. The drop in body temperature increases with decreasing ambient temperature.

(b) Linear regression of 5-HT-induced hypothermia for various power densities at 2450 MHz. Similar to ambient temperature, the magnitude of hypothermia is less with an increasing power density.

$$\frac{0.30\ \frac{^\circ\text{C colonic temp}}{1.0\ ^\circ\text{C ambient temp}}}{0.15\ \frac{^\circ\text{C colonic temp}}{1.0\ \text{mW/cm}^2}} = 2\ \text{mW/cm}^2/^\circ\text{C}$$

That is, a 2-mW/cm^2 increase in the power density of RF-radiation exposure is equivalent to a 1 °C increase in ambient temperature. This is one of the very first attempts to equate ambient temperature and RF-radiation exposure. Most importantly, this quantitative comparison had to be performed in cold-stressed animals.

4.1.9 RF-Radiation Exposure and Behavioral Temperature Regulation

Adair (1980b) trained squirrel monkeys to regulate their ambient temperature by controlling the influx of warm or cold air into an environmental chamber. Under normal conditions the monkeys selected an ambient temperature of 34 to 36 °C. The selected ambient temperature significantly decreases when the animals are exposed to an incident power density of 6 to 8 mW/cm^2 (SAR = 1.1 W/kg). IR radiation of equal power density elicited much smaller changes in the selected ambient temperature. It was concluded that RF-radiation-induced absorption activates thermoregulatory behavior by stimulating internal thermal receptors.

Stern *et al*. (1979) trained cold-exposed rats to press a bar for heat from an IR lamp. When exposed to 2450-MHz radiation at a power density as low as 5 mW/cm^2 (SAR = 1 W/kg), the rate of bar pressing for heat decreased. Furthermore, the rate of bar pressing is inversely related with the RF-radiation power density. The power density levels that elicited changes in the thermoregulatory behavior had no effect on deep-body temperature. Whiptail lizards will move into a microwave field of 93 mW/cm^2 at 2450 MHz to maintain their body temperature above ambient temperature (D'Andrea *et al*. 1977). However, the same animals will maintain an even higher body temperature when allowed to move under an IR lamp.

4.1.10 Unresolved Questions

There are two principal schools of thought in physiologic research: (1) the reductional approach and (2) the holistic approach. Reductionalism determines many properties of an organism by closely examining individual cells, tissues, or organs under *in vitro* conditions, albeit most of the data must be greatly modified or discounted for predicting activity of the cellular elements when they are incorporated into the whole animal. For example, in the field of thermal physiology it is well known that isolated tissues tolerate higher temperatures than organs, which in turn tolerate higher temperatures than the whole organism. The holistic approach to physiology research relies on the classic concept that the whole is greater (or occasionally lesser) than the sum of its parts. These philosophic principles must be considered in an assessment that relies on animal experiments to determine the effects of RF radiation on man.

It has been argued, since rectal temperature may rise 2 to 3 °C with a fever or strenuous exercise, that a 1 °C rise in temperature during RF-radiation exposure can certainly not be unhealthy (Tell and Harlen 1979). This is an example of a break between the reductionalist and the holist; the former attempts to equate two entirely different biologic perturbations (fever or exercise and RF-radiation exposure) that evoke similar effects (increase in body temperature), whereas the latter examines each of the two treatments as unique to the whole organism. During a fever there is a perturbation in the thermoregulatory center in the hypothalamus, causing the subject to vasoconstrict and shiver violently, resulting in a regulated increase in body temperature. During exercise humans and other mammals undergo an initial period of peripheral vasoconstriction. Also, during exercise the thermoregulatory system's sensitivity is increased in anticipation of an elevated thermal load. On the other hand, with RF-radiation exposure, body temperature will increase above the subject's preferred body temperature. The subject responds by increasing the activity of thermoregulatory mechanisms of heat dissipation (see Figure 4-1). By comparison, with fever, the subjects increase their preferred body temperature instead of preventing the rise. Hence, equivalent rises in body temperature from fever vs. RF-radiation exposure differ greatly from a physiologic standpoint. In the former, the system is regulating toward an increase in temperature, whereas in the latter case the system is regulating against an increase. Clearly, internal heating of normal subjects with RF radiation is unusual for the whole organism. The increase in body temperature is not regulated, the body temperature is forced to a higher level, while thermal dissipating motor outputs (Figure 4-1) are activated to counteract the heat load.

From these basic principles of physiologic research it is apparent that information is lacking in the following areas:

- The equivalence of heat loads from normal ambient heating and RF heating. The study by Smialowicz et al. (1980) has scratched the surface of this problem (Figure 4-9). We know from this study that, for the mouse exposed to 2450 MHz, 2 mW/cm^2 is proportional to a 1 °C increase in ambient temperature. It is important to know what this relationship is for larger mammals. Then it would be possible to determine an equivalence between ambient temperature and RF radiation exposure for humans.

- The manner in which neural elements of the thermoregulatory system respond to RF heating. It would be interesting to contrast the neural responses during RF radiation exposure and normal ambient heating.

- Measurement of the SAR of RF radiation while mildly perturbing a physiologic system (Tables 4-2 and 4-3). Few of these study data are available; furthermore, there are few data from studies using identical SAR's for normal heating and RF heating while measuring the magnitude of the physiologic response.

TABLE 4-2. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON THERMOREGULATION

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (total min)	SAR (W/kg)	
Inhibits metabolic rate without changing rectal temperature	Mouse	2450 (CW)	NA*	30	1.6, 5.5, 10.4, 23.6, or 44.2	Ho and Edwards (1977a)
Stimulates heat dissipation in mice	Mouse	2450 (CW)	NA	30	24.6, 30.7, 38.8, or 40.1	Ho and McManaway (1977)
Vasodilation and hyperthermia	Dog	2800 (PW)	165	120 to 180		Michaelson et al. (1961)
Increases core and skin temperature	Rhesus monkey	26	500, 750, or 1000	360		Frazer et al. (1976)
Behaviorally selects a cooler ambient temperature	Squirrel monkey	2450 (CW)	6-8	10	1-2	Adair and Adams (1980b)
Male and female mice of varying size have a lethal dose of approximately 40 J/g	Mouse	2450		3 to 8	~ 80	Rugh (1976b)
This dose level along with electric foot shock is synergistic in promoting increases in core temperature	Rat	2450 (PW)		1	2 and 10	Justesen et al. (1974)
Increases temperature of heart-liver area	Mouse	2450	260	5	30 mW/g	Rotkovska et al. (1973)

(continued)

TABLE 4-2. (continued)

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (total min)	SAR (W/kg)	
Core temperature rises rapidly initially then stabilizes	Rhesus monkey	15, 20, or 25	760-1260	180	NG**	Krupp (1977)
Reduces the rate of bar-pressing for heat when exposed to a cold environment	Rat	2450 (CW)	5	15	10	Stern et al. (1979)
Dose-related increase in core temperature	Rat	2450 (CW)	13-60	120	2-9.6	Lotz and Michaelson (1978)
Increase in body temperature and decrease in serum corticosteroids	Rat	2450 (CW)	20	480	5	Lu et al. 1977
Optimal frequency for raising core temperature	Rat	600 (PW and CW)	20	55	5	D'Andrea et al. (1977)
Increase whole-body evaporative heat loss	Mouse	2450 (CW)	NA	90	29	Gordon (1982a)

[*] NA = Not applicable, because exposures were made in a waveguide system.

[**] NG = Not given.

TABLE 4-3. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON BLOOD FLOW

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (total min)	SAR (W/kg)	
Increases femoral blood flow	Dog	2450 and 27 (CW)	NA*	20	NG**	Siems _et_ _al_. (1948)
Diathermy more than doubles femoral blood flow	Dog	27	NA	15	NG	Wakim _et_ _al_. (1948)
Causes rapid increase in heart apex during ventral exposure	Dog	2450 (CW)	NG	15 to 140	NG	Marks _et_ _al_. (1961)
Increases tail and foot temperature with no change in deep body temperature	Squirrel monkey	2450 (CW)	8-10	5	1.5	Adair and Adams (1980a)
Promotes vasodilation in vessels of skeletal muscle	Human	27	NG	20 to 34	NG	Abramson _et_ _al_. (1957)
Increase in blood flow of extremities	Human	2450 (CW)	NG	1 to 30	NG	Gersten _et_ _al_. (1949)
Increases femoral blood flow along with muscle, subcutaneous, and skin temperature	Dog	3000	NG	15	NG	Leden _et_ _al_. (1947)

*NA = Not applicable.
**NG = Not given.

4.2 NUMERICAL MODELING OF THERMOREGULATORY SYSTEMS IN MAN AND ANIMALS

Ronald J. Spiegel

4.2.1 Heat-Transfer Models

It is important to develop accurate mathematical models to predict the absorption of electromagnetic energy and the thermal response of biological subjects. Mathematical modeling can provide a method for gaining qualitative and quantitative information that may be valuable in explaining and understanding many of the effects measured in experimental animals. More importantly, experimentation on human subjects is often unethical. Thus, to extrapolate RF-field results in experimental animals to equivalent effects in man, one must know thoroughly the dosimetry for both species. This can be achieved by the application of a sophisticated and realistic numerical simulation of the energy absorption and subsequent thermal response of subjects exposed to RF fields.

Several investigators have developed mathematical models to calculate the thermal response of the human body when subjected to different environmental conditions or levels of exercise. The same basic approach can be taken to develop a model to simulate the effect of RF radiation. This model, however, must take into account that RF fields deposit energy nonuniformly in the human. The simple one-dimensional heat transfer models used in the past will not accurately simulate this condition. A short review of these previous attempts to model man in one dimension, however, will provide good background for developing a more general model.

One of the earliest attempts at modeling the human body was made by Pennes (1948), who developed a cylindrical model of a human limb. This model was first used to simulate the human forearm but was later applied to the general case of limbs. The following factors were included in this model: (1) radial conduction, (2) metabolic heat generation, (3) convection to the blood, and (4) environmental exchange by convection, radiation, and evaporation.

Machle and Hatch (1947) introduced the concept of a core-and-shell model by comparing measured values of rectal and skin temperatures representing the core and shell temperatures used in the model. Empirical correlations for radiation, convection, and evaporation were experimentally developed for inclusion in this model. A modification by Kerslake and Waddell (1958) extended the model to include the case of complete skin wetness due to sweating.

Wyndham and Atkins (1960) further extended the core-and-shell model by introducing several concentric cylinders representing the different body layers. This model used a finite difference technique to solve a set of resulting first-order differential equations by an analog computer.

A completely rigorous analytical approach was taken by Hardy (1949), who applied the laws of thermodynamics and heat transfer to the human system. This analysis included radiant exchange with the environment, thermal conduction through concentric cylinders, both natural and forced convection, and evaporation from the skin and lungs. The analysis was accompanied by experimental verification of several of the calculated responses.

Wissler (1961, 1964) modified the models of Pennes and Wyndham and Atkins and combined them to obtain a model of the entire human body. This model subdivided the body into six elements: head, torso, two arms, and two legs. Each of these elements was assumed to have the following: (1) a uniformly distributed metabolic heat generation, (2) a uniformly distributed blood supply, (3) a composition of homogeneous materials, and (4) a geometry of isotropic cylinders. The effects of heat loss through the respiratory system and countercurrent heat exchange between the arteries and veins were also included.

In contrast to the models based on concentric cylinders, Crosbie *et al.* (1963) used an infinite slab model to represent an element of the body. These investigators argued that, by applying this geometry, the physics and physiology of the human system could be better understood and that many uncertainties in previous analyses could be clarified. This model was programmed on an analog computer and verified by experimental observation.

Smith and James (1964) developed another analog model to study thermal stress in man. This model had the following characteristics: (1) metabolic heat production in the working muscles, (2) muscles insulated by a layer of subcutaneous tissue, (3) blood flow from the muscles to the skin, and (4) blood flow between different elements of the body and heart. This model considered radial conduction through three concentric cylinders and countercurrent exchange between the arteries and veins, and it was verified experimentally.

The next major effort at modeling the entire human body was made by Stolwijk and associates at the John B. Pierce Foundation Laboratory. The initial effort by Stolwijk and Hardy (1966) was a model composed of three cylindrical segments, one each for the head, trunk, and extremities. The trunk was divided into three concentric layers: skin, muscle, and core. The head and extremities were divided into two concentric layers: skin and core. In this work, the concept of the body being composed of a controlled system and a controlling system was suggested. These investigators also did a rigorous review to determine accurate thermal properties of the constituents of the human body. This model was then programmed for analysis by an analog computer and compared to experimentally developed parameters.

The 1966 Stolwijk-Hardy model was expanded (Stolwijk and Cunningham 1968; Stolwijk 1969, 1971; Stolwijk and Hardy 1977) to include six segments: head, trunk, arms, hands, legs, and feet. All of these segments were composed of four layers: skin, fat, muscle, and core. The geometry of each was cylindrical except for the head, which was spherical. This model was programmed for analysis by a digital computer and included high metabolic heat production, sweating, blood flow to all layers, and convective and radiant exchange with the environment. Stolwijk's model is the most comprehensive program to date, and several investigators have adapted it to special cases; e.g., Montgomery (1972; 1974a,b; 1975) used the model to study the effects of man immersed in water.

4.2.2 RF-Radiation/Heat-Transfer Models

As discussed earlier, there exist reasonably realistic RF-energy deposition models (see § 3.2.3, Analytical and Numerical RF Electromagnetic Interaction Models) and heat transfer models (see above discussion) for the human body. However, few attempts have been made to combine the two models to predict the body's thermal response under exposure to RF fields. In one study, Emery et al. (1976) determined the thermal effects of a uniform deposition of RF energy for a one-dimensional model of heat conduction. Although this model may yield realistic values for whole-body temperatures, the heating pattern produced by nonuniform deposition of energy may deviate substantially from that produced by uniform absorption; this deviation may occur if various parts of the body (head, arms, legs, etc.) selectively absorb energy from the incident field because of whole- and partial-body resonance. In another study, Guy et al. (1978) used thermographic determinations of the distribution of RF energy in phantom models of man, which were subsequently used to provide input for Emery's one-dimensional thermal model. While this method certainly accounted for the nonuniformity in the RF-energy deposition, it apparently did not account for heat flow along the major axis of the body. This is important, because the primary nonuniformity in the RF-energy deposition will occur along the body's major axis, since the body is much longer than it is thick. Thus, this model will tend to overestimate the temperature profile in the body because the model allows heat flow to occur only from the core to the skin. In reality, as a result of localized RF-energy deposition, heat flow must also occur along the major length of the body.

The most general attempt to date has been the work of Spiegel *et al.* (1980a), who have used block models to calculate the RF-energy deposition in the body with a two-dimensional extension of Stolwijk's model to determine the resulting thermal response of the body. This model allows heat flow from the core to the skin as well as along the major axis of the body. The authors used a transient heat conduction model with internal heat generation and heat dissipation. The internal heat generation is caused by metabolism and absorption of RF energy. The internal dissipation is caused by convective exchange with the cardiovascular system and a combined convective and radiant exchange with the surrounding environment at the surface of the skin. The equation simulating the response is, therefore,

$$\rho c \frac{\partial T}{\partial t} = \nabla (k \nabla T) + \frac{1}{V} (QEM + QM - QE - QR) \qquad (4\text{-}1)$$

where ρ = tissue density

c = tissue specific heat

T = local tissue temperature

t = time

V = tissue volume

k = tissue thermal conductivity

QEM = electromagnetic energy deposition

QM = metabolic heat generation

QE = evaporative heat dissipation in the skin

QR = respiratory heat loss in the lungs

To solve Equation 4-1, the body is divided into several finite elements and this relationship is applied to each element or node. The body is represented by 15 segments, with each segment subdivided into 4 concentric layers -- core, muscle, fat, and skin. The head is modeled by a sphere; the neck, hands, and feet are approximated as single cylindrical segments, the arms and legs are each divided into four cylindrical segments, and the trunk is divided into three cylindrical segments. The radius and length of each of these cylindrical segments are based on dimensions for a standard man (Diffrient et al. 1974). Calculations of heat capacitance, thermal conductance, and density are based on the type of tissue, the surface area, and the volume for each segment and layer.

In this model, the time and spatial derivatives are represented by finite difference approximations, and the resulting system of equations is solved by an iterative procedure in which the initial temperatures are used to compute the temperatures a short time later. These new temperatures are then used to compute the temperatures at the new time and so on until thermal steady-state conditions are reached.

Figure 4-11 shows the relationship of the various thermal conductances for a typical segment that includes four nodes in the finite element analysis.

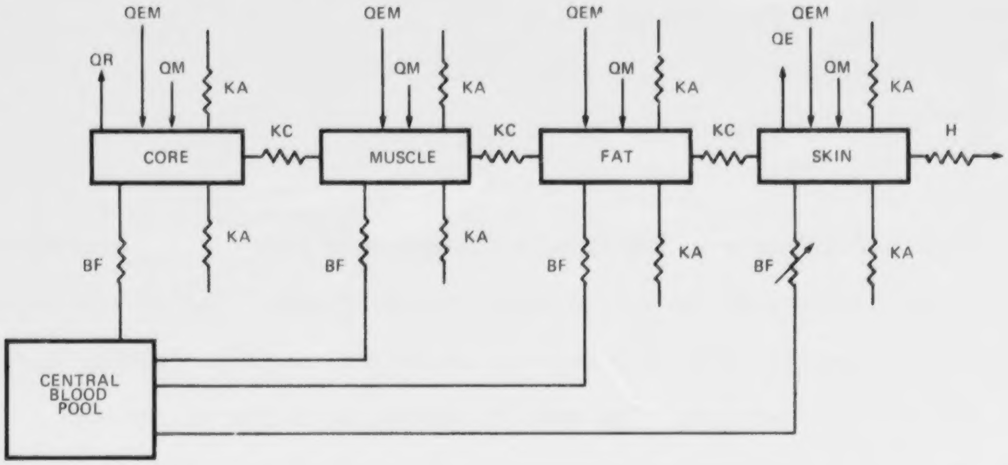


Figure 4-11. Block diagram for one segment of the thermal model.

Each lumped conductance represents heat exchange with the other nodes. The quantities KC and KA represent the radial and axial conductances, respectively, the values of which are determined by layer and segment geometry and by tissue thermal conductivity (Carslaw and Jaeger 1959). Heat exchange between the skin and surrounding environment by convection and radiation is represented by the quantity H, and it is determined in the standard engineering manner as described by Stolwijk (1971). The BF terms designate the amount of heat exchanged by each node and the central blood pool, and they are a function of blood flow. Blood flow rates to all segments, except the skin, are set to basal values (Stolwijk 1971). The skin blood flow rate is controlled by vasodilatation, which is a function of the temperature difference between the local skin temperature and the skin set-point temperature, as well as the difference in temperature between the hypothalamic temperature and its set-point temperature. It is believed that all tissues respond to local temperatures in excess of 40 °C by increasing blood flow. However, the literature does not appear to provide enough information to include this response for all 100 compartments of the model.

The other heat exchange modes shown in Figure 4-11 include metabolic heat production, QM; heat loss by sweat evaporation on the skin, QE; respiratory heat loss in the lungs, QR; and electromagnetic heat input, QEM. The respiratory loss is determined according to Stolwijk, and the model assumes that the expired air has come to thermal equilibrium with the upper trunk core temperature and is saturated. This term enters the equation for thermal balance (Equation 4-1) only at the node that represents the core of the upper trunk segment. Several mathematical models have been proposed to calculate the heat lost by sweating (Emery _et_ _al_. 1976). All are empirical and attempt to best fit experimental data for various conditions, such as for a sedentary subject or for various levels of exercise. This model is based on the detailed work of Stolwijk (Stolwijk 1971, Stolwijk and Hardy 1977). Evaporation basically is controlled by the sweating rate. As with the rate of blood flow, the term that simulates sweating is a function both of the temperature difference between the local skin temperature and the skin set-point temperature and of the difference between the hypothalamic temperature and its set-point temperature. The body develops its own source of heat as a result of metabolic heat production, QM. For a sedentary subject, this value can be at the basal level or can be accelerated by shivering. Shivering is initiated when the body is subjected to a low ambient temperature (< 28 °C for a nude subject) and experiences a chill. Since the air temperature for this study is always in excess of 28 °C, the effects of shivering and vasoconstriction are not included in the analysis. The RF energy input term, QEM, is calculated by a block model comprised of 180 cubical cells of various sizes (Hagmann et al. 1979a).

4.2.3 Numerical Results

To illustrate the model used by Spiegel et al. (1980a), Table 4-4 shows the resulting steady-state temperature distribution in a 70-kg, 170-cm-high human exposed to a plane wave at frequencies of 80 and 200 MHz. The electric field vector is oriented parallel to the major axis of the body (i.e., E polarization). Whole-body resonance occurs for the 80-MHz field, and partial-body resonance occurs in the arms for the 200-MHz field. For the 80-MHz case, an incident power density of 10 mW/cm^2 is used (SAR = 2.25 W/kg). For the 200-MHz field, incident power densities are 10 and 32.5 mW/cm^2 (SAR's = 0.58 and 1.9 W/kg, respectively). As mentioned above, the RF-energy deposition term, QEM, is inserted into Equation 4-1 in a manner prescribed by the 180-cell model.

Note that the distribution of temperatures is quite different in the two cases. For the 80-MHz field, a thermal hot spot (a temperature of around 41.6 °C) is generated in the lower thigh; for the 200-MHz field the hot spot tends to occur in the arms. In addition, note that for the 200-MHz case there is an elevated temperature (40.6 °C) in the neck. Another difference is that the hot spot occurs for an incident power density of 10 mW/cm^2 for the 80-MHz field, while 32.5 mW/cm^2 was required to produce a hot spot for the

TABLE 4-4. STEADY-STATE TEMPERATURES (°C) IN A HUMAN BODY AFTER EXPOSURE TO 80- AND 200-MHz RF FIELDS

		80 MHz		200 MHz			
		10 mW/cm^2		10 mW/cm^2		32.5 mW/cm^2	
Segment	No.	Muscle	Core	Muscle	Core	Muscle	Core
Head	1	36.3	37.4	36.1	37.0	37.0	37.2
Neck	2	38.3	38.9	37.7	38.2	40.6	40.6
Upper trunk	3	37.7	37.3	36.9	36.9	37.6	37.1
Middle trunk	4	38.8	37.5	37.2	37.0	39.3	37.2
Lower trunk	5	38.9	37.8	37.1	37.0	38.4	37.2
Upper humerus	6	34.5	35.9	35.3	36.5	37.0	38.4
Lower humerus	7	34.6	36.0	36.9	38.0	41.2	42.9
Upper forearm	8	34.4	35.7	36.3	37.5	39.8	41.4
Lower forearm	9	34.0	35.0	35.1	36.1	36.9	38.4
Hand	10	36.4	36.6	36.0	36.2	36.4	36.6
Upper thigh	11	39.5	40.3	35.7	37.0	35.8	37.1
Lower thigh	12	40.3	41.6	35.5	36.7	35.7	37.0
Upper calf	13	39.9	41.2	35.7	36.9	36.7	37.9
Lower calf	14	38.4	40.0	35.5	36.4	36.7	37.9
Foot	15	36.4	36.8	35.6	35.8	35.9	36.1

200-MHz case. This occurs because the whole-body SAR is at least four times greater for the 80-MHz field.

As another useful method to present the data, Figure 4-12 graphically shows the time it takes to obtain a hot spot for a given level of incident power density level for the two frequency conditions. The production of a hot spot can be viewed in terms of a strength-duration model; for example, Figure 4-12 shows that the time required to create a hot spot in the lower thigh for an 80-MHz field takes only a few minutes at 50 mW/cm^2, but at 10 mW/cm^2 it will take an hour or more of exposure. In addition, different minimum levels of power density are required to produce hot spots at various body locations. For instance, the rectal temperature profile has an asymptote at a level just above 35 mW/cm^2, but the lower thigh core temperature asymptote occurs around 10 mW/cm^2. For 200-MHz radiation, the lower humerus core temperature was considered, and the intensity-duration curve for this case is shown by the dashed curve.

Based on these results, and as might be expected, the most critical temperature elevations occur at whole-body resonant frequencies. In fact, the rise in temperature is sufficient to produce a hot spot (41.6 °C) in the legs for an incident power density of 10 mW/cm^2. Based on the calculated results, it should again be emphasized that the increased blood flow response for tissue temperatures in excess of 40 °C was not included in the model. Therefore, the model most likely overestimates the magnitude of the temperature rise in the thigh.

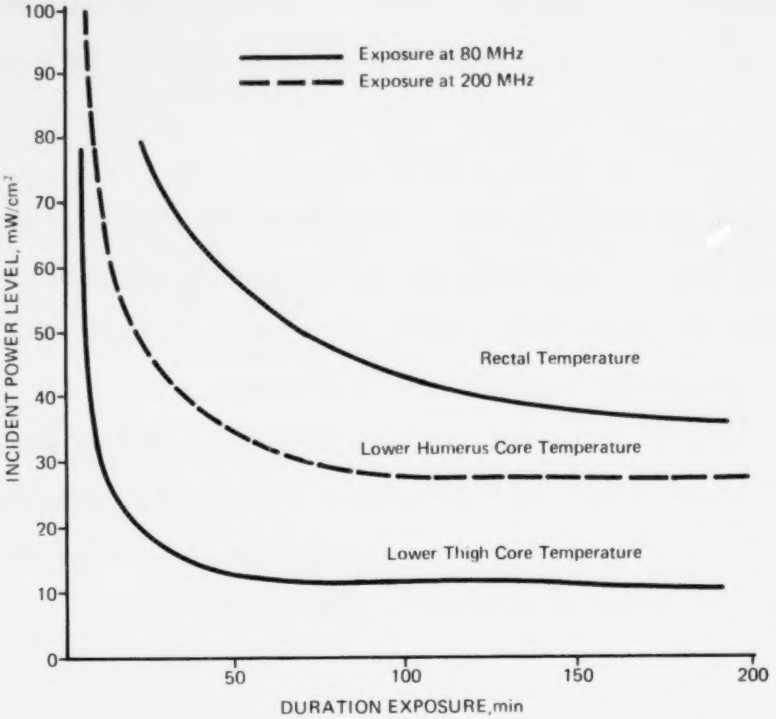


Figure 4-12. Incident power density vs. exposure duration to obtain a hot spot (41.6 °C).

4.2.4 Unresolved Questions

Although the combined RF-heat-transfer model reported here is realistic enough to predict gross effects and trends, the model could be further refined. The most obvious refinement is the extension of the two-dimensional heat transfer model to a three-dimensional simulation. While this extension is numerically straightforward, problems might arise in computer storage requirements and in the computational time needed to generate the heating patterns. In addition, altered tissue blood flow for temperatures in excess of 39 °C has not been implemented in the model. While this modification would be simple, its implementation would require experimentation to quantify the altered blood flow rates.

Another problem is that little is known about the effects of RF energy on the predominant heat-dissipating mechanisms of sweating and vasodilatation. While the empirical models yield results that compare well with experimental measurements from a human subject placed in a room at a controlled temperature and relative humidity, it is certainly open to question whether good agreement between measured and calculated results would likewise be obtained when the thermal load is caused by an RF field. This problem could be resolved by verifying the model experimentally using animal models.

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Biological Effects of Radiofrequency Radiation

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NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the risk of existing and new man-made environmental hazards is necessary to establish sound regulatory policy. Environmental regulations enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our nation's population.

The Health Effects Research Laboratory conducts a coordinated environmental health research program in toxicology and clinical studies. These studies address problems in air pollution, radiofrequency radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory participates in the development and revision of air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is primarily responsible for providing the health basis for radiofrequency radiation guidelines. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator.

The intent of this document is to provide a comprehensive review of the scientific literature on the biological effects of radiofrequency radiation. The purpose of this effort is to evaluate critically the current state of knowledge for its pertinence and applicability in developing radiofrequency-radiation exposure guidelines for the general public.

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ABSTRACT

This document presents a critical and comprehensive review of the available literature on the biological effects of radiofrequency (RF) radiation through 1980. The objective is to determine whether the existing data base can contribute to the formulation of RF-radiation exposure guidance for the general public.

The frequency range of concern in this document is 0.5 MHz to 100 GHz, which includes all the significant sources of population exposure to RF radiation. Research reports that are judged to be credible according to a set of objective criteria are examined for the relation between the RF energy absorbed and the presence or absence of biological effects. The reported consequences of the interaction between RF radiation and biological systems are examined from four perspectives by 1) RF-energy-induced core temperature increases, 2) whole-body-averaged specific absorption rate (SAR), 3) the exogeneous energy burden as a percentage of resting metabolic rate, and 4) actual human experiences documented in epidemiological studies.

The existing data base does lead to tentative conclusions about the relation between RF-radiation exposure and biological effects that may serve as unadjusted upper limits for population exposure guidance; however, the uncertainties and unknowns in the current state of knowledge are potentially significant.

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SECTION 5

BIOLOGICAL EFFECTS OF RF RADIATION

5.1 CELLULAR AND SUBCELLULAR EFFECTS

John W. Allis

The investigation of RF-radiation effects on cellular and subcellular systems is principally an attempt to eludicate specific biochemical mechanisms for the interaction of the radiation with macroscopic biological systems. This approach takes advantage of the relative simplicity of *in vitro* systems, the ability to control variables, the rapid and economical way with which results may be obtained, and the perceived ease of mechanistic interpretation of the results. In practice, however, these advantages are not always realized.

The divisions between molecular, subcellular, and cellular systems are somewhat arbitrary, but for convenience, results presented in this section will be discussed in this format. Examples of each classification are presented in Table 5-1. When investigating molecular and subcellular systems, one normally looks at a single key structure or function where, one hopes, all other variables may be held constant. In these cases, thorough understanding of the end point under study allows the investigator to interpret results more easily in terms of a detailed biochemical mechanism. For instance, if a change in the kinetics of an enzyme-catalyzed reaction is found, the type of inhibition can be determined, the particular molecules involved can be identified, and a hypothesis for the effect can be constructed.

TABLE 5-1. CLASSIFICATION OF CELLULAR AND SUBCELLULAR EXPERIMENTS

Classification	Type of System Studied	Examples of Experimental Measures
Molecular	Purified enzyme preparations	Enzyme activity, binding to small molecules
Molecular	Purified DNA preparations	DNA melting
Subcellular organelles	Membrane-bound enzymes	Enzyme activity
Subcellular organelles	Cell membranes, phospholipid vesicles	Infrared, Raman spectra
Subcellular organelles	Isolated mitochondria	Mitochondrial function
Cellular	Red blood cells	Ion transport
Cellular	Bacteria	Growth, survival, infectivity
Cellular	Isolated neurons	Neuronal firing, membrane potential

In some experiments on intact cells, these conditions can also be approached. An example of this is sodium (Na^+) and potassium (K^+) transport across the red-blood-cell (RBC) membrane. The RBC's limited metabolic activity is geared primarily to performing its main function of transporting oxygen from lungs to tissue. In this case, ion transport across the membrane is linked to the mode of energy production in the cell and very little else, and studies on this system are relatively simple to interpret.

Experiments on most living cells are complicated by complex biochemical systems, many of which have multiple or alternate pathways. Rather than isolated functional changes, broad end points such as growth or genetic changes are often assayed. Here, the investigator tries to use "biological amplification" where, for example, the cell's growth is highly sensitive to disruptions of a critical but unspecified metabolic step, or where a mutant appears that must reproduce over several generations before sufficient numbers are present to be measurable. The investigator also recognizes that the redundancies in a complex system like a living cell may negate any efforts to detect the putative effect.

This inherent complexity makes it difficult to ascribe a detailed biochemical mechanism to effects found. Such effects must be viewed as a starting point from which a mechanism may eventually be deduced. On the other hand, effects on cells can also be used to rationalize or interpret--perhaps even predict--effects in the intact animal.

5.1.1 Effects on Molecular Systems

To obtain insights into possible direct interactive mechanism(s) of microwave radiation at the molecular level, several investigators have attempted to measure changes in biologically important macromolecules exposed in vitro (Table 5-2). Enzyme kinetics studies form a majority of the reports, but a few examine changes in macromolecular structure. In one of the latter, Hamrick (1973) measured DNA melting curves after exposure of calf thymus DNA to 2.45-GHz (CW) radiation for 16 h (SAR = 67 W/kg) and at dose rates to 160 W/kg for 1 h. Temperature was controlled during all exposures, usually at 37 °C, but for some experiments it was maintained at 40, 45, and 50 °C. The intent of the study was to determine if microwaves disrupted hydrogen bonding between the DNA strands of the double helix, thereby affecting the melting curve. The assay was carried out after exposure. In one experiment, any disruption of hydrogen bonding between the strands was preserved by performing the microwave exposure with formaldehyde in the buffer. However, all melting curves were virtually identical to those of unexposed, temperature-matched controls.

In another study of macromolecular structure (Allis 1975), the protein bovine serum albumin (BSA) was exposed to 1.70- and 2.45-GHz (CW) radiation (SAR's ranging from 30 to 100 W/kg). The author recognized that structural changes due to microwave exposure may be reversible. In this study, the problem was attacked by developing an exposure apparatus in which ultraviolet (UV) and visible spectrophotometric measurements could be performed during exposure. The difference in UV absorption between the exposed and unexposed samples was measured directly by using a double-beam spectrophotometer. Differences of this type reflect small changes in the surroundings of certain UV-absorbing amino acids and, in this case, could be interpreted as changes in the structure of the protein. The temperature of the exposed samples was

TABLE 5-2. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON MOLECULAR SYSTEMS

End Point Measured/ Effects	Experimental System	Exposure Conditions				
		Frequency (GHz)	Duration (min)	Exposure Facility (Type)	SAR (W/kg)	Reference
No change in UV difference spectra measured over pH range 2.5-5.5	BSA*	1.70 (CW) 2.45 (CW)	30	Waveguide	30-100	Allis (1975)
UV spectra and binding constants for mononucleotides showed no difference from controls	Ribonuclease	1.70 (CW) 2.45 (CW)	30	Waveguide	39	Allis et al. (1976)
No change in enzyme activity	Glucose-6-phosphate dehydrogenase; adenylate kinase; NADPH cytochrome C reductase	2.45 (CW)	5	Waveguide	42	Ward et al. (1975)
No difference in melting curves	DNA	2.45 (CW)	60, 960	Far field	67, 160	Hamrick (1973)
Inactivation of enzyme; probably temperature inhomogeneity effect at very high doses	Horseradish peroxidase	2.45 (CW)	5, 10, 20, 30, 40	Waveguide	62,500-375,000	Henderson et al. (1975)
Heat inactivation of enzymes found at highest SAR (T = 50 °C), corresponded closely to heat-treated controls	Glucose-6-phosphate dehydrogenase; lactate dehydrogenase; acid phosphatase; alkaline phosphatase	2.8 (PW)	4.5, 18.5	Waveguide	~ 200-500	Belkhode et al. (1974a,b)
Heat inactivation of enzyme found at SAR's > 165 W/kg	Lactate dehydrogenase	3.0 (CW)	20	Waveguide	33-960	Bini et al. (1978)

*BSA = bovine serum albumin.

controlled during exposure, and it was matched by the temperature of the control sample. Temperatures ranged from 24 to 32 °C depending on the SAR value. Spectra were measured immediately upon beginning exposure, and again 30 min later with continuous exposure. The study results showed that no changes in the UV spectrum could be found over a variety of structural states of the protein, implying that structural changes due to microwave exposure could not be inferred.

The ability of microwave radiation to alter enzyme activity has been studied by several workers. Measurements were performed during microwave exposure by two groups, each using spectrophotometric measures of enzyme activity. Ward _et_ _al_. (1975) examined three enzymes (glucose-6-phosphate dehydrogenase, adenylate kinase, and NADPH-cytochrome reductase) exposed to 2.45-GHz (CW) radiation (SAR = 42 W/kg). All exposed and control samples were maintained at 25 °C. Exposure durations were ~ 5 min, during which the enzyme activity was measured. No differences between exposed and control samples were found. Bini _et_ _al_. (1978) followed the activity of lactate dehydrogenase exposed to 3.0-GHz (CW) radiation (SAR's between 33 and 960 W/kg). They demonstrated that the changes found in the enzyme activity were entirely consistent with calculations of thermal inactivation of the enzyme at the temperatures attained. The sample exposed at 33 W/kg was not different from the unexposed control; all other exposures (SAR's ranging from 165 to 960 W/kg) showed evidence of enzyme inactivation.

Belkhode _et_ _al_. (1974a,b) reported the effect of 2.8-GHz square-wave modulated (1-kHz) radiation on four enzymes: glucose-6-phosphate dehydrogenase, lactate dehydrogenase, acid phosphatase, and alkaline phosphatase. Enzyme preparations were analyzed after exposures (SAR's ~ 200 to 500 W/kg on average). Exposures were conducted at 37, 46.7, and 49.7 °C; enzyme activities were compared to the activity of sham-exposed samples at the same temperatures. Activities of the exposed enzymes at each temperature were indistinguishable from the shams.

Henderson _et al_. (1975) reported a change in enzyme activity that was interpreted as an indicator of direct interaction on the enzyme by microwaves. In this experiment, horseradish peroxidase was subjected to 2.45-GHz (CW) radiation (SAR's between 62,500 and 375,000 W/kg) with the sample exposed in a tube (4.7-mm ID) that protruded through a waveguide. The sample tube was surrounded by a concentric cooling jacket, through which an organic coolant was pumped continuously to maintain the temperature at 25 °C. Thermocouples were placed in the sample tube so that the sample temperature could be monitored from positions just outside the waveguide. The total volume of the exposed sample was ~ 0.8 ml. A marked decrease in enzyme activity was found at 62,500 W/kg after 30 min of exposure, and at 187,500 W/kg after 20 min of exposure, even though the temperature was reported never to exceed 35 °C. It is possible that the very high fields present at these SAR's could produce field-specific effects. However, it appears likely that very high local heating occurred in the sample that was responsible for enzyme inactivation. This likelihood is substantiated by the work of Harrison _et al_. (1980) who performed liquid-crystal thermography under similar exposure conditions. Temperature rises of as much as 0.3 °C were recorded within a micropipette suspended in a waveguide and cooled with water circulating through the waveguide. Henderson _et al_. (1975) exposed their samples at 5 to 10 times the levels used by Harrison _et al_.; also, the latter researchers used water as a coolant, which would attenuate the energy reaching the sample much more strongly than would the organic solvent used by Henderson _et al_. A study by Livingston _et al_. (1979) graphically illustrates the effect of temperature gradients during microwave exposure.

The binding of small substrate-like molecules to the enzyme ribonuclease was studied to determine if the binding relationship between an enzyme and substrate could be affected by microwaves (Allis _et al_. 1976). In this work, UV-absorption spectra were measured during exposure to 1.70- and 2.45-GHz (CW) radiation (SAR = 39 W/kg). Measurements were performed immediately upon beginning irradiation and after 30 min of exposure. Neither structural changes in the enzyme-substrate complex nor changes in the binding constants were found. In sum, no consistent effects on molecular systems exposed _in vitro_ to RF radiation have yet been demonstrated.

5.1.2 Effects on Subcellular Organelles

There has been relatively little research on the effects of microwave radiation on subcellular organelles (Table 5-3). The reports included in this document range from work with phospholipid bilayers (i.e., synthetic analogs of cell membranes) to experiments using intact mitochondria, the energy-producing system in eukaryotic (e.g., mammalian) cells. Most of the work to be discussed

TABLE 5-3. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON SUBCELLULAR SYSTEMS

End Point Measured/ Effects	Experimental System	Exposure Conditions				Reference
		Frequency (GHz)	Duration (min)	Exposure Facility (Type)	SAR (W/kg)	
Increase in exchange of strongly bound amide hydrogens in membrane protein measured by IR spectra for SAR > 10 W/kg; No change in α-helix or β-sheet content of proteins	RBC membrane†	1.0 (CW)	30	Stripline	5-45	Ismailov (1977)
No change in activity of membrane bound enzymes measured spectrophotometrically	RBC membrane; mitochondrial inner membrane	2.45 (SW*)	10	Waveguide	26	Allis _et al_. (1979)
No change in activity of membrane bound enzyme measured spectrophotometrically	Endoplasmic reticulum	2.45 (CW)	5	Waveguide	42	Ward _et al_. (1975)
No difference in respiratory activity	Mitochondria	2.45 (CW)	30 to 210	Anechoic chamber far field	17.5, 87.5	Elder and Ali (1975)
No difference in respiratory activity	Mitochondria	2-4 (Swept) 3.4 (CW)	10	Coaxial Airline	1.6-2.3 41	Elder _et al_. (1976)
No change in formation of microtubules	Tubulin (rabbit brain)	3.1 (PW)	15	Far field	112-430	Paulsson _et al_. (1977)
No change in migration of proteins within axonal membrane	Vagus nerve cell	3.1 (PW)	24 h	Far field	~ 10-100	Paulsson _et al_. (1977)
No changes in IR spectra of proteins and nucleic acids in _E. coli_ exposed before drying	Dried film of _E. coli_ cells	3.2 (CW)	8, 10, 11 h	Waveguide	20	Corelli _et al_. (1977)

*SW = Sine-wave modulated.
†RBC = Red blood cell.
#IR = Infrared.

here has not demonstrated effects of microwave exposure at dose rates ranging from 1 to 430 W/kg. Two reports that have indicated an effect do not meet all criteria for inclusion here and are, therefore, discussed with other reports that present unresolved questions.

Two reports describe work with enzymes bound to biological membranes. The study by Ward et al. (1975), discussed above, focused on the enzyme NADPH-cytochrome C reductase, which is loosely bound to the membrane of the endoplasmic reticulum of rat liver cells. Allis et al. (1979) studied adenosine triphosphatase (ATPase) in RBC membranes and cytochrome oxidase in the inner mitochondrial membrane of rat liver cells. The latter two enzymes are thought to be integral parts of membranes. Conditions of the exposure were identical for all three enzymes in that the assay was performed spectrophotometrically during exposure to microwaves. In the latter study the dose rate was 26 W/kg, and the 2.45-GHz radiation was sinusoidally modulated at 16, 30, 90, and 120 Hz. Enzyme activity was not measurably affected by these exposures; a 10- to 15-percent change in enzyme activity would have been required to detect a reliable microwave effect.

Ismailov (1977) investigated the infrared (IR) absorption spectra of proteins in RBC membranes exposed to 1.009-GHz fields (SAR's up to 45 W/kg) and maintained at 25 °C. The samples were exposed for 30 min in aqueous suspension in a stripline, then were dried to a thin film to obtain the IR spectra. No change in α-helix or β-sheet content of the membrane proteins was noted. However, when D_2O (heavy water) was added to the suspension before beginning exposure, application of microwaves was found to increase the degree to which strongly bound amide hydrogens were exchanged. This effect was pronounced at SAR = 45 W/kg but disappeared when the SAR was below 10 W/kg. The increase in accessibility of the poorly exchangeable amide hydrogens indicates that the microwaves disturb the relationship of the protein to its neighboring membrane lipid. A quantitative estimate of the sensitivity of this experiment cannot be made from the spectra shown in the paper.

IR spectra of *Escherichia coli* after exposure to microwaves were also measured (Corelli *et al*. 1977). After 12 h of exposure to 3.2-GHz (CW) radiation (SAR = 20 W/kg), *E*. *coli* were dried to a film, and spectra were measured in the protein and nucleic acid absorption regions. No differences were found. These results are comparable with those of Ismailov (1977) that indicated no changes, but they do not address the conditions for which Ismailov did report effects.

The functional properties of the microtubule assembly system extracted from rabbit brain cells were studied after exposure to 3.1-GHz fields by Paulsson *et al*. (1977). The binding of a drug, colchicine, to the microtubule precursor protein tubulin was measured after exposure to PW microwaves for 15 min at average dose rates of 112 and 243 W/kg (pulse-repetition frequency of 200 Hz, pulse duration of 1.4 μs). Colchicine normally blocks the formation of microtubules, which halts cell division. The normal assembly of microtubules from tubulin exposed for 10 min to PW microwaves, as above, at 430 W/kg was also studied. No noticeable effect on either process was found. The data indicate that a change of about 15 percent in the colchicine binding and about

10 percent in the microtubule assembly measurement would have been noted. Paulsson _et_ _al_. also studied the migration of proteins within the axonal membrane of the rabbit's vagus nerve. In this case the samples were exposed for 24 h (the SAR estimated from their data was 10 to 100 W/kg) at a pulse-repetition rate (PRR) of 100 Hz and a pulse duration of 1.4 μs. The distribution of tritium-labeled protein in the axonal membrane was found to be the same in exposed and control samples. A difference of > 20 percent would have been required for detection in this experiment.

Two papers (Elder and Ali 1975; Elder _et_ _al_. 1976) present results of exposure of rat liver mitochondria to microwave radiation. Both papers examine oxygen utilization by measuring respiratory activity (e.g., respiratory control ratio, ADP to oxygen ratio) under various conditions. These parameters are functional indicators of the energy production system in eukaryotic cells. The earlier paper tested mitochondria kept at 0 °C, or inactive state, during exposure in the far field at 2.45 GHz. The mitochondrial functions were examined after exposure in the active state at 25 °C. (Exposures for periods up to 3.5 h were conducted at SAR's of 17.5 and 87.5 W/kg.) No changes in mitochondrial activity were seen. In the later paper, the disadvantage of exposing inactive mitochondria was overcome by use of a novel flow-through system that coupled a coaxial airline and an oxygen electrode. The mitochondrial suspension was cycled continuously between the airline, where exposure was accomplished, and the oxygen electrode. Samples were exposed to 2.45-, 3.0-, and 3.4-GHz (CW) radiation (SAR = 41 W/kg) and also to radiation at swept frequencies between 2 and 4 GHz (SAR's from 1.6 to 2.3 W/kg). As in the earlier work, no effects of microwave exposure were detected under any condition. In general, a five-percent change would have been sufficient for detection. Other workers have presented data on microwave exposure of mitochondria, either in a form too incomplete for inclusion or in oral presentations. Their findings do not differ from those described here.

5.1.3 Effects on Single Cells

Effects on single cells have been investigated by several researchers (Table 5-4). Transport and related properties of RBC membranes have been studied by three groups. In each case K^+ transport was used as an end point. In the RBC, active (or energy requiring) Na^+ and K^+ transport across the membrane is by the enzyme Na^+-K^+ ATPase (the same enzyme discussed in § 5.1.2, Effects on Subcellular Organelles), and passive transport is through channels in the membrane. Ismailov (1971) exposed human RBC's to 1.0-GHz (CW) microwaves at 45 W/kg and found an increased efflux of K^+ and a concomitant increased influx of Na^+. The Na^+ influx was twice as large, ion per ion, as the K^+ efflux. Exposures were carried out in a coaxial stripline for 30 min, with analysis of the ion content of the supernatant performed afterwards. These results indicate either a reversal of the normal action of the Na^+-K^+ ATPase, or an inhibition of the enzyme, which permitted ion leakage across the membrane to change the Na^+/K^+ ratio. Hamrick and Zinkl (1975) and Peterson _et al_. (1979) have performed similar experiments by exposing RBC's at 2.45 GHz in the far field (SAR's were 3 to 57 W/kg, and ~ 200 W/kg, respectively). Neither study found a difference between the K^+ efflux from microwave-exposed RBC's and conventionally heated RBC's with similar histories of temperature elevation, although Peterson _et al_. did find a difference between unexposed

TABLE 5-4. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON SINGLE CELLS

End Point Measured/ Effects	Experimental System	Exposure Conditions				
		Frequency (GHz)	Duration (min)	Exposure Facility (Type)	SAR (W/kg)	Reference
Increase in RBC electrophoretic mobility 30 min post-exposure (SAR ≥ 10 W/kg)	RBC†	1.0 (CW)	4, 8, 15, 30	Stripline	5-45	Ismailov (1978)
Increase in K^+ efflux and Na^+ influx	RBC	1.0 (CW)	30	Stripline	45	Ismailov (1971)
K^+ transport no different from heat-treated controls; no change in osmotic fragility	RBC	2.45 (CW)	60, 120, 180, 240	Monopole far field	3-57	Hamrick and Zinkl (1975)
K^+ transport no different from controls at corresponding temperatures; no difference in hemoglobin release	RBC	2.45 (CW)	45	Anechoic chamber far field	200	Peterson *et al*. (1979)
Passive transport of Na^+, Rb^+ increased at transition temperature	RBC	2.45 (CW)	60	Waveguide	100, 190 390	Olcerst *et al*. (1980)
Rapid response in change of firing rate of pacemaker neurons which does not correlate with temperature changes in minority of trials	Isolated neuron from *Aplysia*	1.5, 2.45 (CW and PW)	3	Stripline	1-100	Wachtel *et al*. (1975); Seaman and Wachtel (1978)
No change in growth, CFU,* of exposed cultures	*E. coli* *P. aeruginosa*	2.45 (CW)	720	Far field	29-320	Hamrick and Butler (1973)
No change in growth, CFU, of various strains of exposed cultures under several growth conditions	*E. coli*	2.45 (CW)	240	Anechoic chamber far field	0.0075-75	Blackman *et al*. (1975)
No change in survival curves (measuring CFU) of exposed cultures	*E. coli* *B. subtilis* spores	2.45	1	Microwave oven	~ 400	Goldblith and Wang (1967)

(continued)

TABLE 5-4. (continued)

End Point Measured/ Effects	Experimental System	Exposure Conditions				
		Frequency (GHz)	Duration (min)	Exposure Facility (Type)	SAR (W/kg)	Reference
Growth rate slowed; morphological changes found	Chinese hamster lung cells, V79	2.45 (CW)	20	Waveguide	1059	Chen and Lin (1978)
No change in light emission of photoactive bacterium	*P. fischeri*	2.6-3.0 (CW)	~ 22	Waveguide	660 to 5300	Barber (1962)
No effect on colony-forming ability	*E. coli*	2.6-4.0 (CW)	8 h	Waveguide	29	Corelli *et al*. (1977)
Temporary decrease in virulence (> 6 h) of bacteria for its host cells; recovery within 24 h at 37 °C	*A. tumefaciens*	10 (CW)	30, 60 230	Cavity	~ 1	Moore *et al*. (1979)

*CFU = Colony Forming Unit.

†RBC = Red Blood Cell.

rabbit cells maintained at 25 °C compared with those maintained at 37 °C. This difference did not occur with human cells. Ismailov also used temperature controls but did not describe the solution parameters for the cell suspensions. Under certain conditions of chemical concentration, it is possible to reverse the Na^+-K^+ ATPase; however, Ismailov's controls behaved normally, indicating that chemical concentrations in the controls were not unusual. The origin of the discrepancy between these studies is not clear.

Hamrick and Zinkl (1975) and Peterson et al. (1979) measured other end points as well. The former looked at osmotic fragility of the RBC's and concluded that there was no difference. The latter paper gives data on hemoglobin release from RBC's, an indicator of membrane fragility. Again, no differences were found between irradiated and heat-treated RBC's; however, as for K^+ efflux, the unexposed rabbit cells released less hemoglobin at 25 °C than at 37 °C.

In a separate paper, Ismailov (1978) reported increases in the electrophoretic mobility of human RBC's exposed under conditions identical to those in his previously discussed study. The electrophoretic mobility was measured at 10-min intervals after cessation of exposure. The mobility was found to peak at 30 min post-exposure and to return to base line ~ 60 min after exposure. The peak mobility decreased with shorter exposure durations (30, 15, 8, and 4 min). Also, the mobility change decreased as a function of dose rate, disappearing between 5 and 10 W/kg. Although a change in the counter-ion distribution around the cell and possible conformational changes in the membrane proteins were discussed or suggested as possible causes, it remained unclear why these phenomena peaked 30 min after exposure.

Passive ion transport in rabbit RBC's was examined by Olcerst et al. (1980) after exposure to 2.45-GHz (CW) radiation (SAR's at 100, 190, and 390 W/kg). The cells were treated with ouabain to inhibit active transport of Na^+ and K^+ by Na^+-K^+ ATPase, the important enzyme discussed previously in several papers. Exposures took place in a waveguide system in which the sample was placed parallel to the E-field in a cylindrical tube. An organic coolant of low dielectric constant was circulated around the sample in a larger concentric cylinder to maintain the temperature of the sample under exposure. The SAR's were computed from readings of forward and reflected power. The RBC's were pre-incubated with radioactive Na^+ or Rb^+ (the latter is a K^+ substitute). Samples were exposed or heat-treated for 1 h, and the suspending medium was analyzed for radioactivity. Graphs of the logarithm of the efflux vs. inverse temperature were identical except at three transition temperatures, where the slope of these plots changes sharply (see Figure 5-1). At these points, the exposed samples exhibited considerably higher efflux than the heated samples; however, no consistent difference between exposure levels could be established. These results imply that the cell membrane structures responsible for passive ion transport are sensitive to microwave exposure at temperatures where transitions between two states are taking place. Living cells depend on closely regulated ion concentrations for many processes, and serious disruption of these balances could be lethal.

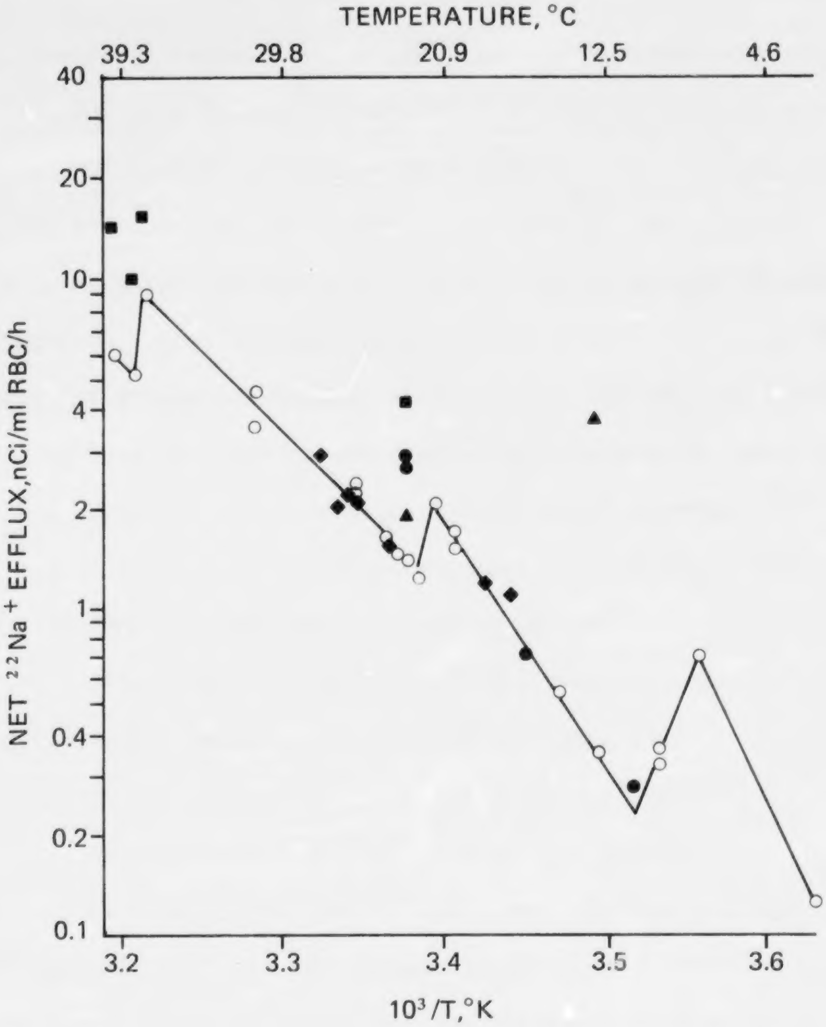

Figure 5-1. Arrhenius plot of Na^+ efflux. Unirradiated temperature controls are represented by open symbols; irradiated samples are represented by darkened symbols. Specific absorption rates are expressed as watts per kilogram (● = 100, ■ = 190, ▲ = 390). Control samples had an average standard error of 0.98 percent. Irradiated samples had an average standard error of 4 percent. (Olcerst et al. 1980).

Many studies have been conducted that focus on a major function of a cellular species as a generalized end point. The reasoning for this approach is that if microwaves disrupt an important metabolic step, the result will be a decline in the ability of the cell to perform its major function. As mentioned earlier, this assumes that no compensating mechanism will operate. A broad spectrum of such end points has been investigated for cells exposed *in vitro*. Some of these are discussed elsewhere: phagocytosis and blastic transformation in lymphocytes are presented in § 5.2, Hematologic and Immunologic Effects; the induction of the antibiotic colicin, along with point mutations in single cells, is discussed in § 5.8, Genetics and Mutagenesis.

Perhaps the ultimate test of a cell's functional ability is growth and survival. Several workers have concentrated on this end point and have investigated the frequency range between 1 and 4 GHz. In general, the results have proved negative. Far-field exposures were conducted (Hamrick and Butler 1973; Blackman *et al*. 1975) on several strains or mutants of *E*. *coli* and on *Pseudomonas aeruginosa*. Samples were exposed in T-flasks or petri dishes, principally at 2.45-GHz (CW) radiation. Growth was measured by assays of colony-forming units (CFU). In both experiments the duration of exposure was sufficiently long (12 and 4 h) that the average cell divided at least once. Blackman *et al*. examined several growth conditions such as lag, log and stationary phases of growth, rich and minimal media, and a "normal" as well as a mutant amino-acid-requiring strain. In each case, no differences between the exposed samples and temperature-matched control samples were found. Hamrick's SAR's ranged from 29 to 320 W/kg with power densities of 60 to 600 mW/cm^2, and Blackman's from 0.0075 to 75 W/kg with power densities of 0.005 to 50 mW/cm^2.

Corelli et al. (1977) exposed E. coli at the end of a waveguide to microwaves swept from 2.6 to 4.0 GHz for 8 h at a dose rate of 29 W/kg. No effect of the microwave exposure was found on colony-forming ability of the bacteria. Goldblith and Wang (1967) exposed E. coli and Bacillus subtilis spores in a microwave oven at 2.45 GHz for periods to 1 min (SAR estimated at 400 W/kg). In this case, microwave irradiation and conventional heating were found to have identical effects on survival.

Chen and Lin (1978) exposed Chinese hamster lung cells, V79, in a waveguide fitted with a micropipette that contained the cell suspension. Temperature was regulated by circulating cooling water through the waveguide around the micropipette. Samples were exposed to 2450-MHz (CW) radiation for 20 min, and the cells were allowed to grow in cultures for 12 days after exposure. The exposed cells were observed to divide at a slower rate and to exhibit a fibroblastic type of growth, in contrast with the controls. These cells were exposed at 400 mW/cm^2 (SAR = 1059 W/kg) under conditions similar to those in which Harrison et al. (1980) found temperature elevations in the sample that were as much as 0.3 °C higher than the cells in the cooling bath. Chen and Lin (1978) state that temperature-treated controls at 38 °C (1 °C higher than the coolant temperature during microwave exposure) did not display the changes observed in the microwave-exposed cells. However, it is not entirely clear whether the changes in the microwave-treated cells were caused by elevated temperatures within the micropipette.

The emission of light by a photoactive bacterium, Photobacterium fischeri, has been used as the end point of one study (Barber 1962), where the bacterial suspension was circulated through a waveguide. The bacteria were undergoing exposure in the waveguide for approximately half the time during a typical 43-min experiment. Bacteria were exposed at several frequencies between 2.6 and 3.0 GHz; the assay was performed 24 h later. In spite of extremely high dose rates, 660 to 5300 W/kg, there were no differences between microwave-irradiated and conventionally heated samples that received parallel treatment.

In the single experiment conducted at 10-GHz frequency, a transient effect was found in the virulence of _Agrobacterium tumefaciens_ towards its normal hosts, potato and turnip disks (Moore _et al_. 1979). This bacterium produces a plasmid, which it injects into the host cells and which is responsible for turning these cells into uncontrolled tumor cells. In this experiment, a suspension of _A. tumefaciens_ was exposed in a petri dish for 30, 60, and 230 min. The longer exposures produced a decrease of virulence near 60 percent with no essential change in the number of viable cells. The effect was unchanged 6 h post-exposure, but virulence returned to normal 23 h post-exposure when the bacteria were maintained at 27 °C. An additional experiment, in which treated and untreated cells were added to the host simultaneously, indicated that the exposed cells were able to compete effectively with untreated cells for binding sites on the host cells. The treated bacteria were always maintained at or below 27 °C during irradiation. From the temperature data in the paper, a dose rate of ~ 1 W/kg and power density of 0.58 mW/cm^2 can be estimated. A possible explanation for this effect, which was not offered by the original authors, is that the plasmid DNA of the _A. tumefaciens_ was incorporated into the major DNA of the bacteria during microwave exposure, preventing injection into the host. Normal growth may have subsequently allowed the plasmid to return to its original state, restoring activity.

In two papers, Wachtel and coworkers (Seaman and Wachtel 1978, Wachtel *et al*. 1975) have examined the effects of microwave irradiation on the firing rate of isolated neurons from the marine gastropod *Aplysia*. Neurons were exposed in a stripline at 1.5- and 2.45-GHz (CW and PW) fields (0.5- to 10-μs duration, 1000 to 15,000 pulses/s). The firing rate of pacemaker neurons and the burst rate of bursting cells were measured during microwave exposure at dose rates between 1 and 100 W/kg. In the majority of cases, the firing rate of pacemaker cells increased with an increase in temperature, and decreased with a decrease in temperature. In a minority of cases, 13 percent, for the pacemaker cells, the microwave irradiation reversed the normal change in firing rate; i.e., the rate decreased or stopped with a microwave-induced increase in temperature. The authors were able to detect slow and rapid components. The slow component, occurring in 30 to 60 s, was correlated with the slow rise of temperature associated with exposure. The rapid component, occurring within 1 s, appeared to correlate with the presence of the microwave field. The rapid component was always found to be a decrease in firing rate in the presence of the field and was never produced by convective heating. Similar but more variable effects were found for the bursting cells. The threshold for the slow component was ~ 7 W/kg, but in one case the rapid component was found at an SAR as low as 1 W/kg. In all cases where effects were found, the firing rates returned to normal when the radiation was terminated and when the temperature was returned to normal. The authors hypothesized that at a dose rate of ~ 1 W/kg, conversion of 0.1 percent of the microwave energy into a polarizing current density across the cell membrane would be sufficient to affect the firing rate of pacemaker neurons.

5.1.4 Unresolved Questions

Several questions remain unresolved in the area of cellular and subcellular effects of microwave radiation. Nearly all of the relevant research is concentrated in a narrow frequency band, between 1.0 and 4.0 GHz. No acceptable studies have been reported for a large portion of the frequency spectrum of concern, 0.5 MHz to 100 GHz.

A related question is that of the role of structured water in the cell. This is presently an active area of research. Questions such as how much water in a cell is structured to a greater degree than "bulk" water, and whether this structure plays an important role in cell metabolism, are as yet unanswered. Three monographs (Alfsen and Berteaud 1976; Drost-Hansen and Clegg 1979; Grant *et al*. 1978) summarize knowledge in this area. Experiments attempting to establish the presence and extent of structured water within biological systems are described, and the dielectric data indicating a possible frequency range for the structured-water resonance are presented. According to the limited information now available, RF radiation is most effective in modifying the state of structured water at frequencies below 1 GHz. As yet no experiments have been conducted that define whether absorption of RF energy by structured water leads to a measurable change in a biological system.

Three of the reports discussed in § 5.1.3, Effects on Single Cells, also raise questions. The explanation offered by Ismailov (1978) for the change in electrophoretic mobility of exposed RBC's is speculative and does not account for the peaking of the phenomenon 30 min post-exposure. These results must be considered an effect of unknown origin until more information is available. The results of experiments by Moore et al. (1979), in which the virulence of *A. tumefaciens* was decreased for more than 6 h after exposure to microwave radiation, suggest reversible functional changes in the organism. In this case, the implications for cellular function after microwave exposure would be broad. However, no other worker has noted a similar effect with other single-cell organisms, and this experiment has not been independently confirmed. Therefore, its significance is unknown at this time.

The results of Wachtel and coworkers (Seaman and Wachtel 1978; Wachtel et al. 1975) are potentially highly significant because they indicate the possibility of a direct interaction between the microwave field and the functioning of the pacemaker neuron (i.e., the rapid effect). Three other workers have obtained supportive results. The documentation in these reports is not sufficiently complete for inclusion in the preceding sections, but they bear mentioning here.

Yamaura and Chichibu (1967) found results strikingly similar to those of Wachtel in ganglia of crayfish and prawn exposed at 11 GHz. The regular firing rate of the ganglia decreased rapidly during microwave exposure, rebounded to a higher than normal rate when the radiation was removed, and then returned to normal. Temperature controls showed only an increased firing rate as the temperature was increased. The authors stated that the SAR was ~ 100 W/kg but did not describe the method of measurement.

Arber (1976) found a hyperpolarization of the resting potential of giant neurons of the mollusk Helix pomatia during exposure to 2.45-GHz (CW) radiation. In this experiment, the ganglion was isolated and mounted in a stripline. The cell potential was measured, as in Wachtel's experiment, by inserting microelectrodes into the neuron. Exposure to microwaves (SAR near 15 W/kg) for 1 h produced a 5- to 10-percent increase in resting potential, followed by a stabilization or slight additional increase over 1 h post-exposure. This result is presumably caused by a change in the Na^+-K^+ balance in the cell. When Arber treated the cells with ouabain (post-exposure), which inhibits Na^+-K^+ ATPase, he found that part of the hyperpolarization could be accounted for by the action of this enzyme under the influence of microwaves. The remainder was attributed to changes in passive ion transport.

Pickard et al. (1980) have recently presented results in which single cells from Chara braunii and Nitella flexilis, plants from the family Characeae, exhibited a large step increase in voltage when exposed to 0.1- to 5-MHz (PW) radiation (pulses were of 250-ms duration, pulse interval was 6.3 s). These authors also found a fast and slow component where the slow component correlated with a temperature rise in the sample. The fast component was frequency dependent and disappeared abruptly at ~ 10 MHz. The authors suggest that the fast component is produced by rectification of the oscillating electric field by the cell membrane. The fast component disappeared into noise at ~ 667 V/m and may have been an effect of intense fields.

The results of these four studies indicate a possibility of a direct microwave interaction with the electric potential across the cellular membrane of all living cells. This kind of interaction would have broad significance in the functioning of all cells and, in particular, cells of the nervous system.

Additional studies have been conducted recently that have not yet been sufficiently documented to include in the previous sections. However, because of their potential importance, they are discussed here. The first two reports concern microwave effects on phospholipid bilayers, whereas the third is concerned with changes in growth of the yeast *Saccharomyces cerevisiae* exposed at frequencies between 41 and 42 GHz.

Tyazhelov *et al*. (1979a) have exposed a phospholipid membrane formed between two chambers containing solutions of NaCl or KCl. An antibiotic that forms pores through the membrane was added to facilitate passage of Na^+ or K^+. Conductance was measured across the membrane while 4-s pulses of 900-MHz radiation were delivered at between 125 and 280 V/m (field strength in the aqueous medium). The results showed a change in conductance under exposure that is consistent with temperature rises of 12 °C, but the temperature of the NaCl or KCl solutions did not vary by > 0.5 °C. However, information concerning the exposure system is insufficient to judge whether serious inhomogeneities in energy deposition, and thus similar inhomogeneities in the temperature distribution, were likely. It is not possible to estimate an SAR from the information presented.

Sheridan et al. (1979) have presented at meetings, but so far have not published, results of Raman spectroscopy on single- and multi-lamellar phospholipid vesicles exposed to 2.45-GHz (CW) radiation. No change was found in the Raman bands of single layered vesicles. In contrast, the data for multi-lamellar vesicles indicate that the hydrocarbon tails of the phospholipids were undergoing a temperature-dependent phase transition at a point where the bulk temperature was too low for the transition to have begun. The change was reported to be equivalent to a temperature difference of ~ 2 °C at an exposure of 25 mW/cm^2. The bulk temperature of the sample in these experiments was measured by a unique method. Small ruby crystals were suspended in the sample, and the shifts in the Raman bands of the crystal were measured and compared with calibration curves. This appears to be an accurate method for temperature determination. The origin of this effect is unknown, but if a similar effect were found in naturally occurring membranes, it could have an impact on the functioning of the biological membrane.

Keilmann and coworkers (Grundler et al. 1977; Keilmann 1978; Grundler and Keilmann 1980) have demonstrated that S. cerevisiae exhibits an enhanced or inhibited growth rate when exposed at certain closely spaced frequencies between 41.60 and 41.80 GHz. For instance, they found a 10- to 15-percent increase in growth rate at 41.64 and 41.68 GHz, and a 20-percent decrease at 41.66 GHz. The experiments were conducted using a unique waveguide termination that was dipped into a suspension of yeast cells. In a typical experiment, 24 W were dissipated in the yeast-cell suspension, and the authors estimated a maximum exposure intensity of about 10 mW/cm^2. However, because of the unusual nature of the waveguide termination and the high attenuation of high-frequency radiation by aqueous samples, SAR values are not determinate. Sample temperature was monitored and was within 0.5 °C of the desired 32 °C. Equivalent temperature controls were performed, and the authors believe that changes of the observed magnitude could not be purely temperature effects. This contention appears reasonable, since the growth rate both increased and decreased at the same levels of incident energy but at different exposure frequencies. The decrease is difficult to explain, based on the author's reports of no observable temperature rise. If, however, a localized temperature of > 37 °C (> 5 °C above the controlled temperature) were attained close to the waveguide termination, then the decrease could be explained solely on the basis of temperature. There are scanty reports from the Soviet literature that present results similar to those of Keilmann and coworkers.

In summary, the available literature on cellular and subcellular effects of microwaves does not yet definitely establish whether effects unrelated to elevation of temperature exist at dose rates on the order of 1 W/kg. Several investigators have reported effects, but a majority have not found effects unrelated to temperature variations. In some cases, the results conflict. In other cases, the effects found are equivocal. Effects of elevated temperature may not be clearly eliminated, or, as in the case of neuronal firing rate, the change in the rate may occur only in a minority of cases (Seaman and Wachtel 1978). The question of heat-induced temperature rises must always be carefully considered when dealing with the biological effects of exposure to microwave radiation. In cellular systems, a principal effect is to increase the rates of all biochemical reactions. This includes the rate of denaturation of proteins and DNA (Lehninger 1975) and the rate at which bases are removed (Lindahl and Nyberg 1974) and mutations occur (Bingham et al. 1976) in DNA. When temperature is raised to a certain level, often ~ 43 °C, cell functions become so disrupted that the cell's capacity to repair the damage is exceeded and the cell dies. The effect of a rapid heating rate is less clear. Some disruption of cell function may be expected from a rapid temperature rise, even if the critical temperature, e.g., 43 °C, has not been reached. Whether this disruption is fully reversible has not been well documented. RF-radiation exposure can produce such high heating rates, especially from high peak, low average power pulses. Effect of nonuniform heat deposition is probably the most difficult aspect to account for when evaluating the effects of exposure to RF radiation.

The effects presented in this section are sufficiently well established to warrant continued concern and effort. The effects of microwave radiation on the electrical properties of the cell are potentially the most significant. Four separate experiments have demonstrated these effects. All cells use the electrical potential across the cell membrane in their life functions, and perhaps the most important cells are those of the nervous system. Microwave effects have been found in the functioning of the nervous system and in behavior, as will be discussed in following sections.

At this time, nearly all of the effects documented for cellular and subcellular systems are observed in intact cells. This could imply that a living cell is required for the necessary interaction with microwave radiation to occur. Or, it may be that the right questions are not being asked about the subcellular level, perhaps because the level of understanding and instrumentation capabilities are as yet too limited. Although the primary mechanism(s) of interaction other than heating the water medium have not yet been defined, some useful directions are indicated by the results reviewed here. There also appear to be valuable correlations between some of the effects at the cellular level with those at higher levels of organization.

5.2 HEMATOLOGIC AND IMMUNOLOGIC EFFECTS

Ralph J. Smialowicz

Over the years, a considerable number of reports has appeared in the literature dealing with the effects of RF radiation on the hematologic and immunologic systems of animals. For the most part, the responsible investigators have been motivated by a concern for the possible adverse health effects of exposure to RF radiation. Studies in which animals have been exposed at different frequencies and intensities have shown inconsistent changes in elements of both biological systems. In some instances, a thermal burden to the exposed animal has been credited with the observed changes, whereas in others, a "nonthermal" (i.e., lack of measurable elevations of temperature) or direct (i.e., athermal or field-specific effects) interaction of RF radiation with the blood and blood-forming systems has been suggested as the causative mechanism for the observed effects. In any case, the final interpretation of RF-induced changes must consider many variables that affect the interaction of RF radiation with the biological entity. As has been noted previously, variables such as body shape and mass, radiation frequency, duration of exposure, field intensity, specific absorption rate, energy distribution, orientation of the body in the field, ambient environmental conditions, area of the body exposed, and field modulation may all influence the final results. Variability of response among species and strains as well as between sexes must also be considered.

This section critically reviews the reported effects of RF radiation on the hematologic and immunologic systems of laboratory animals. From this review the following general conclusions can be drawn:

- Partial or whole-body exposure of animals to RF radiation may lead to a variety of changes in the hematologic and immunologic systems. One of these changes most consistently found is an increase in lymphocyte formation and activity.

- Transient changes in peripheral blood composition, probably caused by redistribution of blood cells and hemoconcentration, were reported; effects on the immune system have often turned out to be transient.

- Several reports describe a causal relationship between increased core temperature and hematologic and immunologic changes.

- Many of the reported effects of RF radiation on the hematologic and immune systems are similar to those (a) resulting from a stress response involving the hypothalamic-hypophyseal-adrenal axis, or (b) following administration of glucocorticoids.

- That an increase in rectal temperature is not observed after exposure to RF radiation does not preclude a thermal interaction that the animal is able to compensate for and control.

- Localized heating or "hot spots" in organs critical to the hematopoietic and immune systems may occur following the production of thermal gradients that are unique to RF-energy absorption by biological specimens.

- There is a lack of convincing evidence for a direct interaction of RF radiation with hematologic and immunologic systems in the absence of some form of thermal involvement.

- There is presently no convincing evidence from animal studies for adverse alterations in the hematopoietic or immune systems at RF-radiation intensities comparable to average environmental levels.

For convenience, this section is divided into two general topics: hematologic effects and immunologic effects. These two topics are further subdivided into reviews of studies in which cellular components of these systems have been exposed *in vitro* and of studies dealing with *in vivo* exposures to RF radiation.

5.2.1 Hematology

Hematology is the study of the anatomy, physiology, and pathology of the blood and blood-forming tissues. The hematopoietic system is comprised of a variety of cells and cell products. In fetal life, the production of blood cells occurs in the liver, spleen, and bone marrow. After birth this function is limited largely to the bone marrow, which produces red cells (erythrocytes), white cells (neutrophilic, eosinophilic, and basophilic granulocytes; lymphocytes; and monocytes), and platelets. Each of these cell types performs specific functions that are essential to life. For example, mature erythrocytes transport O_2 and CO_2 to and from tissues, granulocytes and monocytes phagocytize invading microorganisms, and lymphocytes are involved in immune responses. These functional cells are all descendants of progenitors (stem cells) that reside within the bone marrow. Blood-cell formation consists of two essential processes, proliferation and differentiation; progenitor cells proliferate in the bone marrow and then differentiate into red and white cells. As the process of cell differentiation progresses, the capacity for cellular proliferation decreases. Impairment of either of these processes may lead to dysfunctions in the hematologic system that may be life threatening.

5.2.1.1 *In Vivo* Studies--

A paucity of information on the health effects of RF-radiation exposure from clinical and epidemiological studies has led to studies of effects on the hematologic systems of laboratory animals (Table 5-5). Many of the early investigations on the blood-forming system of laboratory animals employed power densities of 10 mW/cm^2 and higher. For example, Deichmann *et al*. (1964)

TABLE 5-5. SUMMARY OF STUDIES CONCERNING HEMATOLOGIC EFFECTS OF RF-RADIATION EXPOSURE*

Effects	Species	Exposure Conditions				References
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Increased: WBC, lymphs, PMN, RBC, Hct, and Hgb	Rat	24,000 (PW)	10 20	1 x 180 1 x 420	$3.0^\dagger$	Deichmann et al. (1964)
No change	Dog	24,000 (PW)	24	400 x 400-900	$1^\dagger$	Deichmann et al. (1963)
No change Decreased: RBC, WBC and lymphs Increased: PMN	Rat	3,000 (PW)	10 40 100	216 x 60 20 x 15 6 x 5	$2^\dagger$ $8^\dagger$ $20^\dagger$	Kitsovskaya (1964)
Decreased: lymphs and eosin Decreased: WBC, PMN, and eosin Decreased: WBC, lymphs, and eosin Increased: PMN Decreased: lymphs Increased: PMN	Dog	2,800 (PW) 2,800 (PW) 1,280 (PW) 200 (CW)	100 165 100 165	1 x 360 1 x 120 1 x 360 1 x 360	$4^\dagger$ $6^\dagger$ $4.5^\dagger$ $25^\dagger$	Michaelson et al. (1964)
No change	Mouse	800	43	175 x 120	$12.9^\dagger$	Spalding et al. (1971)
Increased: lymphs and mitotic index of lymphoid cells	Guinea pig	3,000 (CW or PW)	3.5	120 x 180	$0.5^\dagger$	Baranski (1971 and 1972a,b)
Increased: RBC, Hct, and Hgb	Rat	2,400 (CW)	10	30 x 120	$2^\dagger$	Djordjevic and Kolak (1973)
No change	Rat	2,400 (CW)	5	90 x 60	$1^\dagger$	Djordjevic et al. (1977)
Increased: eosinophils	Rabbit	2,450 (CW)	10	180 x 1380	1.5	McRee et al. (1980a)
Increased: WBC, CFU Decreased: ^{59}Fe uptake	Mouse	2,450 (CW)	100	1 x 5	$70^\dagger$	Rotkovska and Vacek (1975)

(continued)

TABLE 5-5. (continued)

Effects	Species	Exposure Conditions				References
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Accelerated recovery following x-irradiation; increased erythropoiesis and myelopoiesis	Mouse	2,450 (CW)	100	1 x 5	$70^{\dagger}$	Rotkovska and Vacek (1977)
Accelerated recovery from x-irradiation	Dog	2,800 (PW)	100	1 x 3600	$4^{\dagger}$	Michaelson et al. (1963)
Increased: PMN and RBC Decreased: lymphs Accelerated recovery room x-irradiation	Chinese hamster	2,450 (CW)	60	1 x 30	$28^{\dagger}$	Lappenbusch et al. (1973)
Increased: lymphs Decreased: PMN (Not reproduced consistently)	Rat (Perinatal exposure)	425 (CW)	10	47 x 240	3-7	Smialowicz et al. (1982)
No change	Rat (Perinatal exposure)	2,450 (CW)	5	57 x 240	1-5	Smialowicz et al. (1979a)
No change	Rat (Perinatal exposure)	100 (CW)	46	57 x 240	2-3	Smialowicz et al. (1981a)
No change	Quail egg	2,450 (CW)	30	1 x 1440	14	Hamrick and McRee (1975)
Decreased: Hct, WBC, and lymphs	Rat (young)	2,736 (PW)	24.4	35 x 240	5-25†	Pazderova-Vejlupkova and Josifko (1979)

(continued)

TABLE 5-5. (continued)

Effects	Species	Exposure Conditions Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	References
No change	Mouse	2,450 (CW)	30	22 x 30	22	Smialowicz *et al*. (1979b)
Decreased: lymphs Increased: PMN	Mouse	26 (CW)	8610		13[†]	Liburdy (1977)
Decrease in CFU for erythroid and granulocyte-macrophage series	Mouse	2,450 (CW)	15	9 x 30	10	Huang and Mold (1980)
Reduction in CFU granulocyte-macrophage precursors exposed *in vitro*	Mouse	2,450 (CW)	60-1000	1 x 15	120-2000	Lin *et al*. (1979b)

*WBC = white blood cell, PMN = polymorphonuclear leukocytes, RBC = red blood cell, Hct = hematocrit, Hgb = hemoglobin, and CFU = colony-forming unit.

[†] SAR estimated.

reported significant leukocytosis, lymphocytosis, and neutrophilia in rats following 7 h of exposure to 24,000-MHz (PW) microwaves at an average power density of 20 mW/cm^2 (SAR estimated at 3 W/kg). One week following exposure, peripheral blood values returned to normal. Rats exposed for 3 h at 10 mW/cm^2 displayed the same changes and returned to normal after 2 days (SAR estimated at 1.5 W/kg). Increases in circulating erythrocytes, hemoglobin concentration, and hematocrit were observed in two of three strains of rats (Osborne-Mendel and CFN) exposed to 24,000-MHz fields at 10 or 20 mW/cm^2. However, in Fischer rats exposed under the same conditions, there was a reduction in the number of circulating erythrocytes and a reduction in hematocrit and hemoglobin concentration. In another experiment, Deichmann _et al_. (1963) exposed two dogs to 24,000-MHz (PW) fields at an average power density of 24 mW/cm^2 (SAR estimated at 1 W/kg). One dog was exposed for 20 months, 6.7 h/day, 5 days/week; whereas the second dog was exposed for 20 months, 16.5 h/day, 4 days/week. No significant changes were observed in blood volume, hematocrit, hemoglobin, erythrocytes, total and differential leukocytes, blood cholesterol, or protein-bound iodine. The only symptom attributed to the exposure was a slight loss of body mass.

Kitsovskaya (1964) exposed rats to 3000-MHz (PW) radiation at 10, 40, or 100 mW/cm^2 for various periods of time (SAR estimated at 2, 8, and 20 W/kg, respectively). No changes were found in rats exposed at 10 mW/cm^2; at 40 and 100 mW/cm^2, however, the number of peripheral blood erythrocytes, leukocytes, and lymphocytes decreased, while granulocytes increased. These blood changes did not return to normal until several months after cessation of exposure.

The apparent discrepancy between the results of Deichmann et al. (1964) and Kitsovskaya (1964) may be partially explained by the work of Michaelson et al. (1964). These investigators reported that the hematopoietic effects of 2800- and 1280-MHz (PW) fields depend on the frequency, intensity, and duration of exposure. For example, dogs exposed to 2800-MHz fields showed a marked decrease in circulating lymphocytes and eosinophils after 6 h at 100 mW/cm^2 (SAR estimated at 4 W/kg). This exposure resulted in a 1 °C mean increase of rectal temperature. Neutrophils remained slightly increased at 24 h, while eosinophils and lymphocyte values returned to normal levels. After a 2-h exposure at 165 mW/cm^2 to 2800-MHz fields (SAR estimated at 6 W/kg), there was a slight leukopenia, neutropenia, and definite hemoconcentration. These changes were accompanied by a rectal temperature rise of 1.7 °C. Eosinopenia was still evident 24 h after this exposure. General leukocytic changes were more apparent following exposure of dogs to 1280-MHz (PW) fields or to 200-MHz (CW) radiation. After exposure of dogs at 1280 MHz for 6 h at 100 mW/cm^2 (SAR estimated at 4.5 W/kg), a leukocytosis and neutrophilia were observed. After 24 h the neutrophil level was still increased above pre-exposure levels. Lymphocyte and eosinophil values were slightly depressed following exposure, but at 24 h they were slightly higher than initial values. A 6-h exposure to 200-MHz (CW) fields at 165 mW/cm^2 (SAR estimated at 25 W/kg) caused a marked increase in neutrophils and a slight decrease in lymphocytes. After 24 h this trend was more evident. Michaelson et al. (1964) suggested that the results indicated a stress response of the exposed animals in the hypothalamic and/or adrenal axis that was brought about by a thermal stimulation from RF-radiation exposure.

Spalding et al. (1971) exposed mice to 800-MHz fields at an average power density of 43 mW/cm^2 (SAR estimated at 10.7 W/kg) for 2 h/day, 5 days/week, for a total of 35 weeks. These investigators found no changes in blood erythrocytes, leukocytes, hematocrit, or hemoglobin concentrations. It is interesting that these investigators did not detect changes in the peripheral blood picture of exposed mice, despite the thermal burden that was being placed on these animals. Four mice died from "thermal effects" following the 33rd and 34th RF-radiation exposures.

Effects produced at levels at or below 10 mW/cm^2 (SAR estimated at 0.5 to 2.0 W/kg) have also been reported. For example, Baranski (1971, 1972a,b) exposed guinea pigs and rabbits to 3000-MHz (CW and PW) microwaves at an average power density of 3.5 mW/cm^2 (SAR estimated at 0.5 W/kg) for 3 months, 3 h daily. At this power level, the body temperature of the animals was not elevated. Observations were made of increases in absolute lymphocyte counts in peripheral blood, abnormalities in nuclear structure, and mitosis in the erythroblastic cell series in the bone marrow and in lymphoid cells in lymph nodes and spleen. No changes were observed in the granulocytic series in peripheral blood. Shifts in peripheral blood cells were found to correlate with changes in the cellularity of the spleen and lymph nodes. An increase in the mitotic index and in the percentage of cells incorporating ^3H-thymidine was observed in the spleen and lymph nodes of exposed animals.

Djordjevic and Kolak (1973) exposed rats to 2400-MHz (CW) fields at 10 mW/cm^2 (SAR estimated at 2 W/kg) 2 h/day for 10 to 30 days. Body temperature in rats exposed under these conditions increased by 1 °C within the first

30 min of exposure and remained at this level throughout the exposure period. Hematocrit, hemoglobin concentration, and circulating erythrocytes increased during the 30-day exposure. Fluctuations in the various leukocyte populations were also observed. The authors suggested these changes were caused by the thermal effect of microwaves. In a more recent study, Djordjevic _et al_. (1977) found no significant difference in any of several hematologic end points for rats exposed to 2400-MHz (CW) microwaves at 5 mW/cm^2 (SAR estimated at 1 W/kg) for 1 h/day during a 90-day period.

Recently, McRee _et al_. (1980a) reported significant decreases in eosinophils and a lowering of albumin and calcium in blood from rabbits immediately following chronic exposure to 2450-MHz fields. In this study, rabbits were exposed 23 h daily for 180 consecutive days to 2450-MHz (CW) radiation at a power density of 10 mW/cm^2 (SAR = 1.5 W/kg). No change in hematologic parameters was observed 30 days after termination of exposure (i.e., depression in eosinophils seen immediately following exposure had normalized); however, a significant decrease in albumin/total globulin ratio was observed in the blood of exposed rabbits at this time. The authors contend that, because only 3 of the 41 blood-chemistry parameters measured immediately after exposure were significantly different ($P < 0.05$), and because this observation is close to that expected by chance, further validation of these changes is warranted.

Rotkovska and Vacek (1975) reported changes in hematopoietic cell populations of mice following a single 5-min exposure to 2450-MHz (CW) radiation at an intensity of 100 mW/cm^2 (SAR estimated at 70 W/kg). The response of microwave-exposed mice was compared with that of mice placed in a warm-air chamber at an ambient temperature of 43 °C for 5 min. Both treatments caused a rise in rectal temperature > 2 °C. A leukocytosis occurred in mice under both conditions; however, the time course for the leukocytosis and the response of hematopoietic stem cells differed between the two treatments. Following RF-radiation exposure, a decrease in the total cell volume of the bone marrow and spleen was observed, and the number of hematopoietic stem cells in bone marrow and spleen, as measured by the colony-forming unit (CFU) assay, increased. Incorporation of ^{59}Fe in the spleen decreased 24 h after RF-radiation exposure. On the other hand, the exposure to heat caused a decrease in the CFU's in bone marrow and spleen and an increase in the percentage of ^{59}Fe incorporation. Rotkovska and Vacek concluded that the different effects of RF radiation and externally applied heat on the hematopoietic stem cells indicate that biological effects caused by high intensities of RF radiation may not necessarily be related only to increases in internal temperature. They indicated that their results suggest a possible "direct" effect. This study is significant because it demonstrates a marked difference in the kinetic response of the hematopoietic system to two forms of heat stress. Consequently, these differences must be considered in the interpretation of RF-radiation-induced changes in the hematopoietic system.

Subsequently, Rotkovska and Vacek (1977) studied the effect of microwaves on the recovery of hematopoietic tissue following exposure to x-irradiation. Mice exposed to x-rays at 300 to 750 rads were then exposed to 2450-MHz (CW) microwaves for 5 min at 100 mW/cm^2 (SAR estimated at 70 W/kg). The combined treatment resulted in an accelerated recovery of hematopoietic tissue, a heightened erythropoiesis and myelopoiesis, and an increased survival rate compared with x-irradiated mice. The increase in the number of endogenous hematopoietic colonies in the spleens of the x-irradiated mice after microwave exposure supports Rotkovska and Vacek's earlier (1975) observation of an elevation in the number of stem cells in the spleens of intact mice after microwave exposure alone. These investigators suggested that RF radiation may influence the mechanisms that activate the pool of stem cells, either by improving the repair of sublethal radiation damage or by increasing the proliferative capacity of stem cells that survive x-irradiation. The authors concluded that this acceleration of the processes of repairing radiation damage in hematopoietic cells after thermogenic doses of RF radiation depended on the stage of intracellular repair at the time of RF-radiation exposure. In earlier work, Michaelson *et al*. (1963) reported that simultaneous exposure to x-rays and microwaves (2800 MHz, PW modulated, 100 mW/cm^2, SAR estimated at 4 W/kg) caused an accelerated recovery of the hematopoietic function in dogs. Thomson *et al*. (1965) reported that pretreatment of mice with RF radiation (2800 MHz, PW modulated, 100 mW/cm^2, SAR estimated at 70 W/kg) reduced the mortality after x-irradiation (800 rads). The 30-day lethality was 40 to 55 percent among mice given single or multiple RF treatment prior to x-irradiation, compared with 76 percent lethality in mice not pretreated with RF radiation. Exposure of Chinese hamsters to RF radiation (2450 MHz, CW, 60 mW/cm^2, SAR estimated at 28 W/kg, for 30 min) 5 min after x-irradiation (725 to 950 rads) significantly increased the x-ray LD_{50}^{30} dose compared with exposure of animals to x-rays only or with exposure to RF radiation before irradiation (Lappenbusch *et al*. 1973). Lappenbusch *et al*. reported that the radioprotective effect of RF radiation appears to be associated with a delayed decrease in the number of circulating white blood cells, reduced period of decreased cell density, and complete replenishment of white blood cells within 30 days following the dual treatment. Exposure to RF radiation either alone or combined with x-ray exposure increased the relative number of neutrophils, reduced the relative number of lymphocytes, and slightly increased the number of circulating red blood cells. On the other hand, animals exposed first to RF radiation and then to x-rays demonstrated a more severe leukocyte picture than hamsters x-irradiated only; in these animals, leukocyte counts decreased faster, and the animals developed leukopenia.

The effect of exposure to RF radiation on circulating blood cells of developing rats has been studied by Smialowicz et al. (1979a, 1982). Rats were exposed pre- and post-natally to 425-MHz (CW) fields at 10 mW/cm^2, 4 h daily up to 41 days. Because the animals were growing, SAR's ranged from 3 to 7 W/kg. No consistent changes in blood values were observed in exposed compared to sham-irradiated control rats (Smialowicz et al. 1982). Rats exposed under the same regimen but to 2450-MHz (CW) fields at 5 mW/cm^2 (SAR estimated at 1 to 5 W/kg) also showed no difference in circulating erythrocyte count, leukocyte and differential counts, or hematocrit and hemoglobin concentration when compared with sham-irradiated controls (Smialowicz et al. 1979a). Rats exposed to 100-MHz fields at 46 mW/cm^2 (SAR estimated at 2 to 3 W/kg) pre- and post-natally as above showed no change in blood parameters compared with controls (Smialowicz et al. 1981a).

Recently Pazderova-Vejlupkova and Josifko (1979) reported decreases in the hematocrits, number of leukocytes, and absolute numbers of lymphocytes in young rats exposed to 2736-MHz (PW, 395 Hz, 2.6-μs pulse width) microwaves at 24.4 mW/cm^2 for 7 weeks (5 days/week, 4 h/day). The means of body mass of rats at the beginning and at the end of the 7-week exposure period was 65 and 350 g, respectively (SAR estimated at 5 to 25 W/kg). These changes disappeared within 10 weeks after termination of exposure. The activity of alkaline phosphatase in neutrophils increased during the first week of irradiation but decreased transiently after the irradiation. In a similar experiment by the same authors (data not given), in which adult rats were exposed for 14 weeks to 3000-MHz (PW, 300 Hz, 2.5-μs pulse width) microwaves at 1 mW/cm^2 (SAR estimated at 0.2 W/kg), no difference was observed in hematologic parameters between exposed and control rats.

Hamrick and McRee (1975) examined the effect of RF radiation on developing birds. Quail eggs were exposed for 24 h during the second day of incubation to 2450-MHz (CW) fields at 30 mW/cm^2 (SAR = 14 mW/g). At 24 to 36 h after hatching, quail chicks were examined for gross deformities, changes in organ weight, and hematologic changes. No significant effects due to RF exposure were detected.

In another study, Smialowicz et al. (1979b) exposed mice to 2450-MHz (CW) fields at 30 mW/cm^2 (SAR = 22 W/kg) for 30 min on 22 consecutive days. These mice showed no significant difference in circulating-erythrocyte count, leukocyte and differential counts, or hematocrit and hemoglobin concentration compared with sham-irradiated controls. In this experiment, mice were maintained in an environmental chamber where temperature, humidity, and air flow were continuously controlled. Under the conditions of this study, the RF radiation did not significantly elevate rectal temperatures of exposed mice. In contrast, when mice were exposed to thermogenic levels (2 to 4 °C rise in rectal temperature) of 26-MHz (CW) radiation, 8610 mW/cm^2 (SAR estimated at 13 W/kg), a decrease in the number of circulating lymphocytes and an increase in circulating neutrophils were observed immediately after exposure (Liburdy 1977). These mice were held in a chamber that lacked a continuous turnover of air. Liburdy (1977) reported that this shift reached its peak 3 h after exposure. The numbers of circulating lymphocytes and neutrophils were reported to return to normal, pre-exposure levels 55 to 96 h after exposure. On the other hand, mice exposed at high ambient temperatures (79 °C) in a vented, dry-air oven showed an increased number of circulating lymphocytes and neutrophils for a 12-h period after exposure. It appears, therefore, that the response of circulating leukocytes to exogenous thermal loading depends on the means by which the body is heated. These results are similar to those reported by Rotkovska and Vacek (1977) and indicate that the heating properties of RF radiation differ from those of conventional modes of tissue heating.

Recently Huang and Mold (1980) reported that bone marrow (cultured *in vitro*) from mice exposed to 2450-MHz (CW) fields at 15 mW/cm^2 (SAR = 10 W/kg) for 30 min on 9 consecutive days had significantly fewer ($P < 0.05$) CFU's of both the erythroid and granulocyte-macrophage series. No data were presented on the peripheral blood counts of any of these blood cells that would confirm or expand the information gathered in the CFU assay.

5.2.1.2 *In Vitro* Studies--

Lin *et al*. (1979b) reported a reduction in the number of CFU's (granulocyte and macrophage precursor cells) formed by bone marrow cells exposed *in vitro* to 2450-MHz fields at 60 to 1000 mW/cm^2 (SAR's at 120 to 2000 W/kg). This reduction in colony formation was reported to be dose dependent and occurred without a significant rise in the temperature of the cell suspension. The authors indicate that their results point to a direct effect of microwave radiation on these hematopoietic precursor cells. Although these results are interesting, the in situ application of fields as intense as those required to produce the observed effects would certainly cause gross thermal injury to the tissue.

In summary, levels of RF radiation that cause an increase in body temperature elicit changes in the hematopoietic system that can for the most part be ascribed to a thermal stress response. Changes in the blood of animals exposed to RF radiation at intensities below those that cause an increase in core temperature suggest a similar stress-response mechanism. The failure to record an increase in core temperature does not preclude that the animal is compensating for the added thermal energy by thermoregulatory mechanisms. Indeed, lack of a temperature change indicates that thermoregulation is operating. The response elicited by RF-radiation-induced heating, however, appears to differ from that of conventional heating because of the differing internal heating patterns of this form of radiation.

5.2.2 Immunology

The immune system is comprised of myriad mechanical, cellular, and humoral components that act as the body's defense against various pathogenic microorganisms, viruses, and neoplasias. The immune system is divided into the humoral element, such as antibodies and complement, and the cellular elements, which are composed of the lymphoid and phagocytic cells. The cellular elements of the immune system are also part of the hematologic system. The phagocytic cells responsible for engulfing and digesting certain microorganisms are the neutrophils or polymorphonuclear leukocytes (PMN's) and the monocytes or macrophages. In the presence of antibodies and complement, neutrophils are aided in engulfing and digesting invading organisms. The monocyte is also a phagocytic cell. Monocytes move into an area in which an infection has begun and then differentiate into macrophages. Macrophages can be "activated" to kill certain microorganisms (e.g., intracellular, facultative bacteria such as _Mycobacteria tuberculosis_ and _Listeria monocytogenes_, viruses, and fungi) through the interaction of certain subpopulations of lymphocytes, such as the T lymphocytes.

The other cellular components of the immune system are the lymphocytes. These cells are broadly divided into two groups, the B lymphocytes and the T lymphocytes. Although these cells are similar morphologically, they are different functionally; B and T lymphocytes can be distinguished by the presence of unique antigens or receptors on their membrane surface. Both T and B lymphocytes are believed to originate in the bone marrow and then to proceed through various stages of development and differentiation, maturing into functional cells of the immune system.

The B lymphocyte, or bursa-equivalent lymphocyte, is responsible for humoral immune responses. The B lymphocytes, after appropriate stimulation by antigens, proliferate and undergo morphological changes and develop into plasma cells that actively synthesize and secrete antibodies.

The T lymphocyte, or thymus lymphocyte, is processed through the thymus after leaving the bone marrow. Classically cell-mediated or T-lymphocyte responses include protection against viruses, fungi, and several bacteria. T lymphocytes are also involved in reactions such as delayed hypersensitivity or contact hypersensitivity and rejection of tumors and foreign tissues such as transplants (allografts). Cell-mediated reactions are so named because these reactions, which operate by specifically sensitized T lymphocytes, can be transferred by these cells to normal animals. B-lymphocyte-mediated humoral responses, in contrast, are transferable by serum.

Each element of the immune system--the T and B lymphocytes and macrophages--plays a cooperative role in defending the host against infection and disease. A delicate balance exists wherein the immune system is prevented from reacting to its own tissues to avoid autoimmune reactions. The alteration or dysfunction of any of these elements may lessen the host's ability to combat infection or may lead to autoimmune disease. However, because of adaptability and redundancy in the immune system, the host can survive subtle perturbations. Consequently, although subtle effects on the immune system may be generated by physical or chemical agents, all such effects may not lead to clinically significant immune dysfunctions.

5.2.2.1 *In Vivo* Studies--

A summary of *in vivo* studies concerning immunologic effects of RF-radiation exposure is presented in Table 5-6.

Effects on adult animals--One of the most consistently found RF-radiation-induced changes in the hematopoietic system is the increase in lymphocyte formation and activity following exposure of animals of several species to RF radiation at various frequencies (Baranski 1971, 1972a,b; Czerski 1975). Consequently, there have been several studies of the effects of RF radiation on lymphocytes and the immune system. In a study reported by Czerski (1975), mice were exposed 2 h daily to 2950-MHz (PW modulated) microwaves at 0.5 mW/cm^2 (SAR estimated at 0.5 W/kg) for 6 to 12 weeks. After 6 weeks, there was a large increase in the relative number of lymphoblasts in the lymph nodes of exposed mice. In another series of experiments (Czerski 1975), rabbits were exposed 2 h/day, 6 days/week for 6 months to 2950-MHz (PW) microwaves at 5 mW/cm^2 (SAR estimated at 0.8 W/kg). After culturing for 7 days *in vitro*, peripheral blood lymphocytes from these animals were found to undergo an increase in "spontaneous lymphoblastoid transformation." Maximal increases occurred after 1 to 2 months of exposure; the transformation rate then returned to base line and rose again 1 month after an irradiation had been terminated. Miro *et al*. (1974) continuously exposed mice to 3105-MHz (PW) microwaves over a 145-h period at an average power density of 2 mW/cm^2 (SAR estimated at 2 W/kg. No description was given of how animals were fed or watered. An increase in lymphoblastic cells in the spleen and lymphoid areas of exposed mice was observed. A somewhat similar response was observed (Huang *et al*. 1977) in lymphocytes cultured from Chinese hamsters that were exposed to 2450-MHz

TABLE 5-6. SUMMARY OF STUDIES CONCERNING IMMUNOLOGIC EFFECTS (*IN VIVO*) OF RF-RADIATION EXPOSURE

Effects*	Species	Exposure Conditions				References
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Increase in lymphoblasts in lymph nodes and increased response to SRBC	Mouse	2,950 (PW)	0.5	42 x 120	$0.5^{\dagger}$	Czerski (1975)
Increase in "spontaneous" lymphoblast transformation of cultured lymphocytes	Rabbit	2,950 (PW)	5	24-48 x 120	$0.8^{\dagger}$	Czerski (1975)
Increase in lymphoblasts in spleen and lymphoid tissue	Mouse	3,105 (PW)	2	6-8700	$2^{\dagger}$	Miro *et al*. (1974)
Increased transformation of unstimulated cultured lymphocyte and decreased mitosis in PHA-stimulated lymphocyte cultures	Chinese hamster	2,450 (CW)	5, 15, 30 or 45	5 x 15	2.3, 6.9, 13.8, or 20.7	Huang *et al*. (1977)
Transient decrease and increased response of cultured lymphocytes to PHA, Con A, and LPS	Mouse	2,450 (CW)	5 or 15	1-17 x 30	3.6 or 10	Huang and Mold (1980)
Increased mitosis of PHA-stimulated lymphocytes	Rhesus monkey	10-27 (PW)	1320	1 x 30	0.4-2.0†	Prince *et al*. (1972)
Increase in CR^+, Fc^+, and Ig^+ spleen cells. Increased response to B-cell mitogens. Decrease in primary response to SRBC	Mouse	2,450 (CW)	--	1 or 3 x 30	14	Wiktor-Jedrzejczak *et al*. (1977a,b,c)

(continued)

TABLE 5-6. (continued)

Effects*	Species	Exposure Conditions Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	References
Increase in Cr$^+$ and Fc$^+$, spleen cells	Mouse	2,450 (CW)	--	1 x 15 1 x 30	11.8 5	Sulek et al. (1980)
Increase in response of cultured lymphocytes to T- and B-cell mitogens	Rat	2,450 (CW) 425 (CW)	5 10	57 x 240 47 x 240 (Perinatal exp)	1-5 3-7	Smialowicz et al. (1979a, 1982)
No change	Mouse	2,450 (CW)	5-35	1-22 x 15 or 30	4-25	Smialowicz et al. (1979b)
No change	Rat	100 (CW)	46	57 x 240	2-3	Smialowicz et al. (1981a)
Increase in T and B lymphocytes in spleen Decrease in DTH	Mouse	26 (CW)	800	1 x 15 or 10 x 15	5.6†	Liburdy (1979)
Reduction of lymphocyte traffic from lung to spleen	Mouse	2,600 (CW)	5 or 25	1 x 60	3.8 or 19	Liburdy (1980)
Decreased response to PWM	Rabbit	2,450 (CW)	10	180 x 1380	1.5	McRee et al. (1980a)
No change	Quail	2,450 (CW)	5	12 x 1440	4.03	Hamrick et al. (1977)
Decrease in tumor development	Mouse	2,450 (CW)	- (near-field application)	11-14 day of gestation or 11-14 & 19-45 x 20	35	Preskorn et al. (1978)
Decreased granulocytic response	Rabbit	3,000 (CW)	3	42 to 84 x 360	0.5	Szmigielski et al. (1975)

(continued)

TABLE 5-6. (continued)

Effects*	Species	Exposure Conditions				References
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Tumor regression and increase in antitumor antibodies and anti-BSA	Rabbit	13.56	(near-field application)	1 x 10-15	(local hyperthermia)	Shah and Dickson (1978b)
Tumor inhibition and immune stimulation	Rat	2,450 (CW)	200W	3 or 6 x 45	(local hyperthermia)	Szmigielski _et al_. (1978)
Increased tumoricidal activity in lymphocytes and macrophages	Mouse	1,356	600-900	1 x 5	(local hyperthermia)	Marmor _et al_. (1977)
Tumor regression	Mouse	3,000 (CW)	40	1-14 x 120	28[†]	Szmigielski _et al_. (1977)
Increase in lung cancer colonies and inhibition of contact sensitivity to oxazolone	Mouse	2,450 (CW)	50	4, 7, 10 or 14 x 120	36[†]	Roszkowski _et al_. (1980)
Decrease in response to BSA	Rabbit	1,356	(near-field application)	3 x 60	(local hyperthermia)	Shah and Dickson (1978a)

*SRBC = sheep red blood cells, PHA = phytohemagglutinin, Con A = concanavalin A, LPS = lipopolysaccharide, CR$^+$ = complement-receptor positive, Ig$^+$ = immunoglobulin positive, Fc$^+$ = Fc portion of immunoglobulin, DTH = delayed-type hypersensitivity, PWM = pokeweed mitogen, BSA = bovine serum albumin.

†SAR estimated.

(CW) microwaves for 15 min on 5 consecutive days at 5 mW/cm^2 (SAR = 2.3 W/kg) without a detectable rise of rectal temperature. Increased transformation to lymphoblastoid forms in the absence of mitogens was maximal in cultures from hamsters exposed at 30 mW/cm^2 (SAR = 13.8 W/kg). Irradiation at this power density caused a 0.9 °C rise in rectal temperature of exposed hamsters. Mitosis of lymphocytes cultured in the presence of the mitogen phytohemagglutinin (PHA), however, was depressed in cells obtained from hamsters exposed at 5, 15, 30, or 45 mW/cm^2. These effects were reported to be transient and reversible; control levels were again observed after 5 to 10 days (Huang *et al*. 1977).

More recently, Huang and Mold (1980) reported an oscillating response of spleen cells to PHA, concanavalin A (Con A), and lipopolysaccharide (LPS) from mice exposed to 2450-MHz fields at 15 mW/cm^2 (SAR = 10 W/kg) for 30 min. Mitogen responsiveness decreased significantly after 2 days of exposure, returned to normal after 4 days of exposure, and was significantly increased for all mitogens after 9 days of irradiation. Responsiveness to mitogens tended to return to normal or to fall to subnormal levels after 17 days of exposure. In contrast, when mice were exposed at 5 mW/cm^2 for 30 min on 5 consecutive days, a significant increase in the response to LPS was observed, whereas no change was observed in LPS responsiveness to exposure at 15 mW/cm^2 for 5 days. When macrophages were removed from spleen-cell suspensions of mice irradiated at 15 mW/cm^2 for 9 days, the responsiveness to LPS was greater than the already increased spleen-cell responsiveness without macrophage removal. However, addition of macrophages from the RF-irradiated mice to spleen-cell cultures from nonirradiated mice caused a significant decrease in responsiveness to LPS. The authors suggest that macrophage activation (macrophages from irradiated mice displayed increased spreading and increased phagocytosis of latex particles _in vitro_) by microwaves may be responsible for inhibiting LPS responsiveness.

Prince _et al_. (1972) reported the opposite effect in rhesus monkeys. These investigators found an enhanced mitotic response of peripheral blood lymphocytes stimulated _in vitro_ with PHA from monkeys 3 days following a 30-min exposure to 10.5-MHz (PW) radiation at 1320 mW/cm^2 (SAR estimated at 0.4 W/kg). Enhancement of mitosis of cultured lymphocytes from monkeys similarly exposed to 19.27- and 26.6-MHz were also reported. Also reported were increases in circulating lymphocytes that ranged from 4 to 47 percent above pre-exposure levels. At a frequency of 26.6 MHz (SAR estimated at 2 W/kg), the rectal temperature of monkeys following exposure was reported to increase by 2.5 °C above pre-exposure levels.

The particular susceptibilities of lymphocytes to RF radiation has led to an examination of the effects of this form of radiation on the immune response. For example, Czerski (1975) reported that mice exposed for 6 weeks to 2950-MHz (PW) microwaves at 0.5 mW/cm^2 (SAR estimated at 0.5 W/kg) had significantly greater numbers of antibody-producing cells and higher serum antibody titers following immunization with sheep red blood cells (SRBC's). Interestingly, mice that were exposed for 12 weeks did not show this increased responsiveness. More recently, Wiktor-Jedrzejczak _et al_. (1977a,b,c) exposed mice in a rectangular waveguide to 2450-MHz radiation for 30 min at an average dose rate near 14 W/kg. At 3, 6, 9, and 12 days after a single or multiple exposures, mice were tested for (1) the relative frequency of T and B splenic lymphocytes, (2) the functional capacity of spleen cells to respond to T- and B-cell-specific mitogens, and (3) the inability to respond to SRBC's (a T-dependent antigen) or dinitrophenyl-lysine-Ficoll (DNP-lys-Ficoll, a T-independent antigen). A single 30-min exposure induced a significant increase in the proportion of complement-receptor-positive (CR^+) lymphocytes in mouse spleens that peaked 6 days after exposure. This effect was further enhanced by repeated (three) exposures, which also produced a significant increase in the proportion of immunoglobulin-positive (Ig^+) spleen cells (Wiktor-Jedrzejczak 1977a). A significant increase in the proportion of Fc-receptor-positive (FcR^+) cells in the spleens was also observed 7 days after a single 30-min exposure (SAR = 13.7 W/kg). However, no change in the number of Ig^+ cells in spleens of these mice was observed (Wiktor-Jedrzejczak 1977c). The type and combination of surface receptors (CR, Ig, Fc) expressed on splenic B cells represent different maturational stages in B-cell development. Wiktor-Jedrzejczak _et_ _al_. (1977a,b,c) were unable to demonstrate any change in the total number of theta-antigen-positive (θ^+) T cells in the spleens of mice following a single or multiple exposure to 2450-MHz microwaves. No change was detected in the _in_ _vitro_ spleen-cell response to stimulation by the T-cell-specific mitogens PHA and Con A or by pokeweed mitogen (PWM), which stimulates both T and B cells (Wiktor-Jedrzejczak _et_ _al_. 1977a). The response to the B-cell-specific mitogens lipopolysaccharide (LPS), polyinosinic polycytidylic acid (Poly I C), and purified protein derivative (PPD) of tuberculin, however, was significantly increased over controls following a single exposure. These results clearly correlate with the observed changes in the proportion of cells bearing different surface markers. These authors (1977a) noted that RF irradiation did not stimulate lymphoid-cell proliferation per se but rather appeared to act as a polyclonal B-cell activator, which led to an early maturation of noncommitted B cells. They also found a significant decrease in the primary immune response to SRBC's, a thymus-dependent antigen, in mice that had been immunized just prior to the first exposure to RF radiation. They suggested that this decreased response may result from the nonspecific stimulation of some cells by RF radiation to mature before they are activated by antigen (SRBC's), thereby increasing the proportion of unresponsive cells.

Recently, Sulek et al. (1980) corroborated this increase in CR^+ and Fc^+ spleen cells in mice 6 days following a 30-min exposure to 2450-MHz fields (average SAR = 12 W/kg). The kinetics for increased frequency of CR^+ cells in the spleens of irradiated mice showed an initial increase 3 days following exposure that persisted for 5 to 6 days and then returned to normal within 9 to 10 days. The threshold for this effect was determined by varying the time of exposure with a constant forward power (0.6 W), or by maintaining a constant time of exposure while varying the forward power (0.1 to 0.78 W). It was shown that a minimum of a single 15-min exposure (11.8 W/kg) or a single 30-min exposure (5 W/kg) caused significant increases in CR^+ cells 3 or 6 days post-exposure. The effect of absorption of multiple subthreshold quantities of microwaves was found to be cumulative only if the exposures occurred within 1 h of one another. The increase in CR^+ cells was found at dose rates ranging from 10 to 18 W/kg for mice within a weight range of 18 to 25 g. The rectal temperature of exposed mice was found to be elevated no more than 0.6 °C above that of sham-irradiated mice. No change in θ^+ (T lymphocytes) cells was observed. In contrast, Huang and Mold (1980) reported a significant increase in θ^+ cells but no change in B cells (Ig^+) of mice exposed to 2450-MHz fields at 15 mW/cm^2 (SAR at 10 W/kg) for 30 min on 9 consecutive days.

Smialowicz _et al_. (1979b) exposed mice to 2450-MHz (CW) fields under far-field conditions for 15 or 30 min daily for periods to 22 consecutive days at power densities from 5 to 35 mW/cm^2 (SAR's at 4 to 25 W/kg). Splenic lymphocyte function was assayed by the _in vitro_ mitogen-stimulated response as measured by ^3H-thymidine incorporation after culture in the presence of T (PHA, Con A, PWM) or B (LPS, PWM, PPD) mitogens. The proportions of T (θ^+) and B (CR^+) splenic cells and the primary immune response of mice to SRBC's were also studied. No difference in the response to mitogens or to SRBC's or in the frequency of T or B cells in spleens was observed in RF-irradiated compared with sham-irradiated mice.

Liburdy (1979) reported that changes in splenic lymphocyte populations similar to those observed by Witkor-Jedrzejczak _et al_. (1977a,b,c) can be produced by exposure of mice to thermogenic levels of 26-MHz radiation. When mice were exposed to 26 MHz at an intensity (800 mW/cm^2, SAR at 5.6 W/kg) that produced a 2 to 3 °C rise in rectal temperature, a relative increase in splenic T and B lymphocytes was observed. Similar responses (i.e., increase in T and B cells) were induced following administration of the synthetic glucocorticoid methyl prednisolone sodium succinate. These results indicate that these RF-radiation-induced changes might represent some form of stress. It is difficult to understand how a 2 to 3 °C rise in rectal temperature would occur in mice irradiated for 15 min (SAR = 5.6 W/kg). A possible explanation is that these mice were restrained in perforated acrylic cages and held in an exposure chamber in which the air was not circulated during this period of irradiation.

In examining further possible mechanism(s) for the shift in lymphocyte populations in the spleens of mice exposed to RF radiation, Liburdy (1980) examined the circulation of lymphocytes in microwave-exposed mice. Mice injected with ^{51}Cr-labeled syngeneic spleen cells were exposed for 1 h at either 5 or 25 mW/cm^2 to 2600-MHz fields (SAR at 3.8 and 19 W/kg, respectively). Controls included sham-irradiated mice, mice held in a 63 °C warm-air oven for 1 h, and mice injected with methyl prednisolone sodium succinate. The distribution of injected cells was determined for the lung, liver, spleen, and bone marrow at 1, 6, and 24 h post-exposure. Exposures at 25 mW/cm^2 caused a 2.0 °C increase in core temperature. This regimen led to a 37-percent reduction in lymphocytes leaving the lung and migrating to the spleen. Also, a threefold increase in spleen lymphocytes entering the bone marrow occurred in this group of mice. A similar pattern of lymphocyte circulation was observed in the steroid-treated group. No change in lymphocyte traffic was observed in mice of the 5-mW/cm^2 or warm-air groups. Liburdy (1980) concluded that these results support the idea that steroid release associated with thermal stress and attempts by the animal to thermoregulate during exposure to RF radiation are responsible for effects on the immune system.

Effects on young animals--RF-radiation effects on the development of the immune response have been studied. Smialowicz et al. (1979a) exposed rats on day 6 of gestation through day 41 to 2450-MHz (CW) fields at 5 mW/cm^2 (SAR at 1 to 5 W/kg). The young animals absorbed microwaves at a higher rate (5 W/kg) than the adults (1 W/kg). In this study the exposed rats had lymphocytes that responded to a significantly greater extent than those from control animals following *in vitro* stimulation by T- or B-cell mitogens. A similar increase in lymphocyte responsiveness was seen in another study in which rats were exposed pre- and postnatally to 425-MHz radiation (SAR at 3 to 7 W/kg, with the neonates absorbing at the latter SAR) for periods to 41 days postpartum (Smialowicz *et al*. 1982). However, lymphocytes from rats exposed perinatally to 100-MHz fields at 46 mW/cm^2 (SAR at 2 to 3 W/kg) showed no change in mitogenic responsiveness (Smialowicz *et al*. 1981a). The results of the two former studies indicate that long-term exposure of developing (especially neonatal) rats to RF radiation at absorption levels higher than those achieved in the latter study may give rise to increased responsiveness of cultured lymphocytes. These results are similar to other reported changes in mammalian lymphocyte responsiveness following RF-radiation exposure (Czerski 1975; Prince *et al*. 1972; Wiktor-Jedrzejczak *et al*. 1977a,b,c). Although the benefits are not known concerning this increased responsiveness to mitogens by lymphocytes from animals exposed perinatally to RF radiation, a recent report by Preskorn *et al*. (1978) indicates that irradiation at this time during development may be beneficial. These investigators exposed mice to 2450-MHz fields (SAR = 35 W/kg) for 20 min either on days 11 through 14 of gestation, or on days 19 through 45 postpartum, or during both periods. On the 16th day postpartum, all mice were implanted with a lymphoreticular cell sarcoma. Mice irradiated *in utero* only (colonic temperature increase of 2.2 °C in dams) showed a lower incidence of tumors (13 percent vs. 46 percent for sham-irradiated mice) 93 days postpartum. In mice irradiated *in utero* and postnatally, tumors initially developed at a lower rate compared with controls; however, after 2.5 months, no difference was observed in tumor incidence between groups. At the end of 4 months, the tumor incidence in irradiated mice was slightly greater than controls (46 vs. 40 percent, respectively). An interesting finding, however, was that both tumor-bearing and tumor-free animals that had been irradiated only in utero lived longer on the average than their respective controls. This result is somewhat similar to that reported by Prausnitz and Susskind (1962), who found that mice briefly irradiated hundreds of times by a highly thermogenic level of RF radiation survived longer than controls.

McRee et al. (1980a) reported that 30 days after termination of a 6-month 23-h daily irradiation to 2450-MHz fields (SAR = 1.5 W/kg) spleen cells from rabbits showed a decreased responsiveness to PWM. Decreased responsiveness to PHA and Con A by these spleen cells was also reported, but responses to PHA and Con A were not statistically different from those of controls. Although these results are interesting, they are not conclusive, because only four exposed and four sham-irradiated rabbits were employed. It should also be noted that both irradiated and sham-irradiated rabbits were transported from one laboratory to another between the termination of RF exposure and spleen-cell assay.

Hamrick et al. (1977) examined the avian humoral-immune response in Japanese quail exposed to RF radiation during embryogenesis. Fertile quail eggs were continuously exposed to 2450-MHz (CW) radiation at 5 mW/cm^2 (SAR = 4.03 W/kg) throughout the first 12 days of development. At 5 weeks of age, quail were immunized with SRBC's, and the levels of anti-SRBC antibodies were determined. No difference was observed in the antibody titers of exposed and sham-exposed quails. The masses of the bursa of Fabricius (site of B-cell production in birds) and spleen were not altered significantly by exposure to RF radiation.

Effects on phagocytosis--RF-radiation-induced effects on phagocytic leukocytes of animals have been reported by Szmigielski et al. (1975). Rabbits were exposed to 3000-MHz fields for 6 h daily for 6 to 12 weeks at 3 mW/cm^2 (SAR estimated at 0.5 W/kg). After the last exposure to RF radiation, rabbits were infected with an intravenous injection of virulent *Staphylococcus aureus*. At periods before and after infection, functional tests of granulopoiesis were performed. The investigators reported a decreased production of mature granulocytes in infected, RF-radiation-exposed rabbits, which was manifested as a more serious illness in these animals.

Summary--Exposure of laboratory animals to RF radiation can lead to changes in the functional integrity of lymphocytes. These cells play an important role in the immune-defense system of man and animals. The significance of the changes caused by RF radiation is difficult to interpret. Although some studies indicate that RF radiation causes an increased responsiveness of lymphocytes (Czerski 1975; Smialowicz et al. 1979a, 1982; Prince et al. 1972; Wiktor-Jedrzejczak et al. 1977a,b,c) and a potentiation of the immune response to antigen (Czerski 1975), others indicate a depression in responsiveness (Huang et al. 1977; Wiktor-Jedrzejczak et al. 1977a; Liburdy 1979; Szmigielski et al. 1975). In most cases these alterations can be attributed to a stress response, since qualitatively similar but quantitatively more pronounced changes are observed at obviously stressful thermogenic levels of RF radiation (Huang et al. 1977; Huang and Mold 1980; Prince et al. 1972; Liburdy 1979) or after administration of glucocorticoids (Liburdy 1979). It is well known that stress alters physiological systems that regulate immunological function. Both immunosuppression and immunoenhancement have been observed to result from stress (Monjan 1981; Blecha et al. 1982), which is not inconsistent with the reported effects of RF radiation on the immune system. Many questions remain about the role of stress in the modulation of the immune system, not the least of which, in the present discussion, deal with RF-radiation-induced stress.

Effects caused by RF-induced hyperthermia--Alterations in the immune system can be produced by RF-radiation-induced hyperthermia. Whole-body microwave-induced hyperthermia has been reported to serve a therapeutic role either alone (LeVeen et al. 1976) or in combination with ionizing radiation (Nelson and Holt 1978). In many cases, the direct destruction of malignant tissues by RF-radiation-induced heating is the ultimate goal. However, in some cases, hyperthermia has led to changes in the immune response. For example, Shah and Dickson (1978b) reported that following local heating of VX2 (carcinoma) tumor-bearing rabbits by a 13.56-MHz field, tumor regression and host cure were observed in 70 percent of the rabbits. Intratumoral temperatures of 47 to 50 °C were achieved within 30 min. Along with tumor regression, cell-mediated immunity--as measured by skin reactivity to tumor extract and dinitrochlorobenzene--markedly increased. A hundredfold increase in serum levels of antitumor antibody and increased response to the antigen bovine serum albumin (BSA) were also observed. In contrast, whole-body hyperthermia led to temporary reduction of tumor growth, followed by a return to an exponential increase in tumor volume and rapid death of the rabbit. This course of events following whole-body hyperthermia was accompanied by abrogation of the enhanced cellular and humoral immune responsiveness, observed following local RF-induced heating.

Szmigielski _et al_. (1978) reported that local heating (43 °C) of the Guerin epithelioma in Wistar rats by 2450-MHz (CW) radiation inhibited tumors and stimulated the immune reaction against the tumor. Other immune reactions stimulated by this treatment were the antibody response to BSA, high reactivity of spleen lymphocytes to the mitogen PHA, and increased serum lysozyme levels as a measure of macrophage activity. Tumor-specific reactions observed were increased cytotoxicity of spleen cells and peritoneal macrophages to cultured tumor cells. Similar results were reported by Marmor _et al_. (1977), who exposed tumors in mice to focal 1356-MHz radiation. The EMT-6 tumor was found to be extremely sensitive to RF heating. The cure rate was a function of temperature and duration of exposure. A 5-min exposure at 44 °C reduced the tumors by almost 50 percent. To determine the effectiveness of RF-induced heating on tumor regression, tumor-cell survival was studied by treating EMT-6 tumors _in situ_. Cell inactivation by RF-radiation-induced heating was similar to that for heating by a hot water bath. The results indicated that direct cell killing could not account for the observed cures, and these investigators suggested that hyperthermia (RF or convection-induced) may stimulate a tumor-directed immune response.

Szmigielski _et al_. (1977) exposed mice bearing transplanted sarcoma-180 tumors to 3000-MHz radiation, 2 h daily on the 1st through 14th day after transplantation, whole-body at 40 mW/cm^2 (SAR estimated at 28 W/kg). This exposure led to a 3 to 4 °C increase in rectal temperature and resulted in a reduction of tumor mass by ~ 40 percent, a reduction enhanced when microwave hyperthermia was combined with Colcemide, Streptolysin S, or both. Colcemide enhances the inhibiting effect of hyperthermia on proliferation of cells _in vitro_ (Szmigielski _et al_. 1976), and Streptolysin S is an antineoplastic agent. Szmigielski _et al_. (1978) suggested that immunostimulation is important in the complex inhibition of tumor growth by increased temperature.

While many have heralded local and systemic hyperthermia as a possible cancer treatment, either alone or in combination with drugs or ionizing radiation, there is evidence that hyperthermia may enhance the dissemination of certain cancers and abrogate the immune response. For example, Roszkowski _et al_. (1980) reported that exposure of mice to 2450-MHz radiation at 50 mW/cm^2 for 4, 7, 10, or 14 days, 2 h daily (SAR estimated at 36 W/kg) caused an increased number of lung-cancer colonies and an inhibition of contact sensitivity to oxazolone (a measure of T-lymphocyte activity) with increased duration of hyperthermia. Shah and Dickson (1978a) exposed normal rabbits either to RF-radiation-induced (13.56 MHz) or to watercuff-local hyperthermia of thigh muscles, which were maintained at 42 °C for 1 h on 3 consecutive days. No alteration in the response to dinitrochlorobenzene challenge was observed. However, the humoral immune response to BSA was significantly depressed. This response was independent of the method and degree of heating. The results indicate that B lymphocytes might be more susceptible to hyperthermic damage than are T lymphocytes.

The above results indicate that if the applied microwaves are of sufficient intensity to cause heating of tissue or of the whole animal, changes in the immune system will follow. And, with heating to any extent, the hypothalamic-hypophyseal-adrenal axis plays a major role in the responses elicited. It is well known that endogenous or exogenous adrenal glucocorticoid hormones affect the immune response. But what of the RF-induced responses reported in the absence of measurable temperature increases or at rates of energy absorption well below that of the resting or basal metabolic rate? Observed changes in the immune response under these conditions are more difficult to explain on a thermal-stress basis, primarily because of a lack of sensitive techniques to detect subtle stress responses. The fact that no increase of rectal temperature occurs after exposure to RF radiation, however, does not preclude that the animal's capablility to compensate for added thermal energy by thermoregulatory mechanisms. RF radiation may also cause focal heating (thermal "hot spots") in organs critical to the immune response.

5.2.2.2 *In Vitro* Studies--

Among the studies in this area (Table 5-7), several have involved attempts to determine if *in vitro* exposure of lymphocytes to RF radiation leads to "direct" changes in the metabolic or functional state of these cells. In an early study, Stodolnik-Baranska (1967) exposed human lymphocytes in culture to 3000-MHz (PW) microwaves at 7 or 14 mW/cm^2. Some lymphocytes were irradiated 4 h/day at 7 mW/cm^2 for 3 to 5 days, while those exposed at 14 mW/cm^2 were irradiated 15 min daily for 3 to 5 days. After 5 days in culture, the microwave-exposed cells were found to have undergone a fivefold increase in lymphoblastoid transformation compared with controls. Czerski (1975) attempted

TABLE 5-7. SUMMARY OF STUDIES CONCERNING IMMUNOLOGICAL EFFECTS (IN VITRO) OF RF-RADIATION EXPOSURE*

		Exposure Conditions				
Effects	Species	Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	References
Increased blastogenesis of exposed lymphocytes in vitro	Human lymphocytes	3,000 (PW)	7 14	3-5 x 240 3-5 x 15	†	Stodolnik-Baranska (1967)
Increased blastogenesis	Human lymphocytes	10,000	5-15	Observed effect only when culture temperature approached 38 °C	†	Baranski and Czerski (1976)
No change in mitogen response to PHA, Con A or LPS	Mouse spleen cells	2,450 (CW)	10	1 x 60, 120, or 240	19	Smialowicz (1976)
No change in mitogen response to PHA	Rat blood lymphocytes	2,450 (CW)	5, 10 or 20	1 x 240, 1440, or 2640	0.7, 1.4 or 2.8	Hamrick and Fox (1977)
No change in viability or growth	Human lymphoblast cell lines (Daudi and HSB_2)	2,450 (CW)	10-500	1 x 15	25-1200	Lin and Peterson (1977)
Decreased macrophage phagocytosis	Mouse macrophage	2,450 (CW)	50	1 x 30	15 J/min	Mayers and Habeshaw (1973)
Liberation of intracellular hydrolytic enzymes and increased death	Rabbit granulocytes	3,000 (CW)	1 or 5	1 x 15, 30, or 60	†	Szmigielski (1975)

*PHA = phytohemagglutinin, Con A = concanavalin A, and LPS = lipopolysaccharide.

†Unable to calculate SAR.

without success to repeat this experiment. But, in a more recent study, Baranski and Czerski (1976) reported that exposure of human lymphocytes to 10,000-MHz fields at power densities between 5 and 15 mW/cm^2 could induce lymphoblastoid transformation (SAR not given). At power densities below 5 mW/cm^2, this effect was not observed, whereas at power levels above 20 mW/cm^2, cell viability decreased. The induction of blastic transformation depended on termination of irradiation (5 to 15 mW/cm^2) at the moment when the temperature of the medium reached 38 °C. These results indicate that the microwave-induced blastic transformation might be caused by a thermal mechanism.

Similar increases in the lymphoproliferative response of cells exposed to temperatures > 37 °C have been reported. Ashman and Nahmias (1978) reported that human lymphocytes, when cultured at 39 °C with the mitogens PHA or Con A, showed an enhancement and earlier onset of ^{3}H-thymidine incorporation compared with cultures incubated at 37 °C. In a similar study, Roberts and Steigbigel (1977) reported that the _in vitro_ human lymphocyte response to PHA and the common antigen streptokinase-streptodornase was enhanced at 38.5 °C relative to 37 °C. Smith _et al_. (1978) reported that the _in vitro_ response of human lymphocytes to PHA, Con A, PWM, and allogeneic lymphocytes was markedly enhanced by culture at 40 °C compared with 37 °C. These studies demonstrate the need to monitor and to control the temperature of cultures exposed to RF radiation. Without adequate temperature data, it is virtually impossible to accept _in vitro_ effects as due to RF radiation itself.

The proliferative response of lymphocytes exposed _in vitro_ to RF radiation appears to be related to culture temperature. Smialowicz (1976) exposed murine splenic lymphocytes to 2450-MHz (CW) radiation for 1, 3, or 4 h at 10 mW/cm^2 (SAR = 19 W/kg). Immediately after irradiation the temperature of the exposed cultures did not differ significantly from that of controls, and cell viability was unchanged. These cells were then cultured for 72 h in the presence of T- or B-cell mitogens, and the proliferative response was measured by ^{3}H-thymidine incorporation. No difference was found in the blastogenic response of microwave-exposed and sham-exposed spleen cells to any of the mitogens employed. In a similar experiment, Hamrick and Fox (1977) exposed rat lymphocytes to 2450-MHz (CW) radiation for 4, 24, or 44 h at 5, 10, or 20 mW/cm^2 (SAR's at 0.7, 1.4, or 2.8 W/kg, respectively). The transformation of unstimulated or PHA-stimulated lymphocytes was measured with ^{3}H-thymidine. No significant differences were found in the proliferative capacity of lymphocytes from exposed and control cultures. The effects of RF radiation on the growth and viability of cultured human lymphoblasts was studied by Lin and Peterson (1977). Human lymphoblasts (cell lines Daudi and HSB$_2$) were exposed to 2450-MHz (CW) radiation in a waveguide for 15 min at incident power densities of 10 to 500 mW/cm^2 (corresponding SAR's were 25 to 1200 W/kg). No temperature increase was observed, even at the highest power density in the capillary tube that held the cell suspension in the waveguide. No change was observed in the viability or growth of microwave-exposed lymphoblasts compared with controls. These studies provide further evidence that in the absence of heating, no change in lymphocyte activity occurs following RF- radiation exposure *in vitro*.

In vitro exposure of macrophages to 2450-MHz fields has been reported by Mayers and Habeshaw (1973) to depress phagocytosis. Monolayer cultures of mouse peritoneal macrophages were perfused with suspensions of human erythrocytes while being simultaneously exposed to 2450-MHz radiation at 50 mW/cm^2. The rate of energy absorption in the sample was 15 J/min. The phagocytic index of exposed cultures was significantly lower than that of the control after a 30-min exposure. Macrophage phagocytic activity returned to normal levels if RF irradiation was discontinued. During irradiation, a 2.5 °C temperature increase was observed; however, the final temperature in the culture vessel in any given experiment reportedly did not exceed 36.2 °C. The investigators concluded that the observed depression of phagocytosis in the irradiated cultures was not thermally induced. The 2.5 °C rise in temperature during irradiation, according to the authors, would have been expected to enhance rather than depress phagocytosis, since optimal phagocytosis occurs at 38.5 °C. The mechanism by which the observed effect occurs is not known; however, heating effects are difficult to dismiss because of an observed 2.5 °C rise in culture temperature. Although the temperature of the suspension medium did not exceed 36.2 °C, thermal gradients of much higher temperature would be expected at the macrophage-glass interface.

An RF-induced effect on granulocyte integrity and viability was reported by Szmigielski (1975). Rabbit granulocytes were exposed *in vitro* to 3000-MHz (CW) radiation at 1 or 5 mW/cm^2 (SAR not given) for 15, 30, or 60 min. Cultures exposed at 5 mW/cm^2 for 30 or 60 min showed increased numbers of dead cells as demonstrated by an increase in nigrosine staining and an enhanced liberation of lysosomal enzymes. Exposure at 1 mW/cm^2 did not cause increased cell death but did lead to a partial liberation of hydrolase enzymes. No change was observed in the temperature of the irradiated cultures. The liberation of acid phosphatase and lysozyme from granulocytes was observed in cell suspensions exposed at 1 or 5 mW/cm^2, both suspensions exhibiting a time- and dose-dependent response.

In summary, exposure of laboratory animals to RF radiation may lead to changes in the functional integrity of leukocytes, which play important roles in the immune-defense system. The significance of the changes caused by RF radiation is difficult to interpret, since many observed effects are transient and reversible. Furthermore, some studies indicate that RF radiation causes immunopotentiation, whereas others indicate immunosuppression. In many cases the observed alterations in the immune system can be attributed to thermal stress, because qualitatively similar but quantitatively greater changes are observed at obviously stressful (highly thermalizing) levels of RF radiation or following the administration of glucocorticoids. A possible explanation for the immunomodulating effects of RF radiation arises from the timing of the measurements of immune responsiveness after subjecting an animal to stress. For example, corticoid-induced impairment of immune responsiveness is commonly followed by homeostatic recovery, then subsequent overcompensation, which may be associated with immunoenhancement.

As for those reports in which measurable elevations of temperature from RF-radiation-induced heating are not detected, a possible role by RF-radiation-induced thermogenesis cannot be dismissed. The failure to detect a measurable increase in tissue or core temperature in RF-irradiated experimental animals through the use of conventional techniques indicates that the animal was able to compensate for the added energy. The role that thermoregulating mechanisms play in affecting the immune response needs further study. There is presently no convincing evidence for a direct effect of RF radiation on the immune system in the absence of a thermal (heating) effect.

5.2.3 Unresolved Questions

Several questions remain unanswered regarding the effects of RF radiation on the hematologic and immunologic systems. Perhaps the most perplexing question is what to make of the many Soviet reports on immunology. In most cases these reports lack sufficient technical detail for adequate critical assessment of reported results. Alterations in the hematopoietic and immunologic systems have been reported in animals exposed to RF radiation at and below 10 mW/cm^2 over periods of weeks to months. Nevertheless, no convincing evidence has been presented to demonstrate a direct effect of RF radiation in the absence of thermal involvement; well defined and planned, chronic (months-to-years), low-level (< 1 mW/cm^2) studies have not been carried out to investigate Soviet claims of possible induction of autoimmune reactions following chronic exposure. Investigations of the possible hematologic and immunologic effects of PW vs. CW irradiation have not been undertaken in response to the claims by Eastern European investigators that PW modulation is more effective than CW irradiation in causing alterations in these systems.

Investigations are lacking that would define possible synergistic effects of other agents or drugs with RF radiation on the hematopoietic and/or immune systems. RF radiation (at hyperthermic doses) has been shown to provide a protective effect against damage by ionizing radiation to the hematologic system. Although this is a beneficial effect of RF radiation, it is not known if the combination of drugs or other physical agents with RF radiation is detrimental.

Another question has been raised that is based on the recent work of Szmigielski et al. (1980), who described the increased incidence of cancer development in mice exposed chronically to 2450-MHz (CW) fields at 5 and 15 mW/cm^2. This is an extremely important piece of work that merits much additional consideration.

5.3 REPRODUCTIVE EFFECTS

Ezra Berman

This section on the reproductive effects of RF radiation is organized into three categories: Teratology (5.3.1), where the treatment is administered to the pregnant dam and observations are then made on the embryo, fetus, neonate, or older offspring; Reproductive Efficiency (5.3.2), where the end point of the experiment occurs in the primary and secondary sex organs of the parent; and Testes (5.3.3), where testicular morphology and function of testes are examined for alterations.

RF radiation has been examined intensively for its potential reproductive effects for a variety of reasons: 1) many reproductive toxicologic tests can be carried out in a simple and inexpensive experimental design after insult by RF radiation, 2) the laboratory techniques used are conventionally acceptable as toxicologic assays, and, especially, 3) detrimental reproductive changes carry an emotional impact.

5.3.1 Teratology

While making judgments on the potential of RF radiation for teratologic manifestations, it is important that the science of teratology and its underlying principles be kept in mind. Wilson (1973) has derived general principles of teratogenesis. These principles are rephrased here to familiarize the reader with the guidelines one should keep in mind when evaluating the available literature, and so that their relevance to RF radiation teratologic investigations is more easily understood.

(1) Susceptibility to RF radiation teratogenesis depends on species, strain, and stage of development at the time of exposure.

(2) There are four indications of abnormal development: death, malformation, retarded growth, and deficient function.

(3) These indications increase in incidence and degree with increasing dosage.

Other aspects of teratology, as a branch of toxicology, are presented in discussing effective experimental design and interpretation. The interpretation of teratologic phenomena is still an art, and there is not full agreement on the significance of certain fetal manifestations after potentially toxic agents are administered. The discussion posits that the list of possible deviations in the conceptus is an order of decreasing degree of severity (death > malformation > growth retardation > functional deficit). Further, the significance that any laboratory animal or system may have as a model of human exposure is not universally accepted among scientists.

An attempt is made to derive from available data three aspects of teratologic toxicology of RF radiation: the presence of a teratologic effect, the generalization of that effect across species, and the dose-response character of that effect. From the evidence presented, we think that the reader will agree with the following statements:

(1) RF radiation can cause teratogenesis in all the mammalian species studied adequately so far if sufficiently high power densities or SAR's are obtained.

(2) Reduced fetal weight seems to occur consistently in rodents exposed gestationally to teratogenic or subteratogenic doses of RF radiation.

(3) Gestational exposure to RF radiation can cause a functional deficit in later life if sufficiently high SAR's are obtained.

5.3.1.1 Nonmammalian Models--

The potential for human teratology is usually sought in mammalian models. But other models that are lower on the phylogenetic scale or cell-culture models are also often elucidative. Workers at the Bureau of Radiological Health of the Food and Drug Administration have used an insect to demonstrate the reproductive alterations due to RF radiation. Pay _et_ _al_. (1978) examined the egg production of female fruit flies (_Drosophila_ _melanogaster_) in response to RF radiation. Using a 2450-MHz waveguide exposure system housed in an environmentally controlled chamber (24 °C, 50 percent relative humidity), these workers determined the survival rate of _D._ _melanogaster_ pupae at SAR's ranging from 400 to 800 W/kg. Approximately 70 percent of the pupae did not survive a 10-min exposure when the rate of energy absorption was 640 W/kg; the temperature of the agar surface on which the pupae rested was 45 °C. If pupae were incubated instead in a 44 °C environment without RF radiation, the death rate was not as severe (50 percent).

The potential for RF-radiation-induced teratology in birds has been examined using the fetal form of birds, the egg, as a model. This is a reasonably popular model since using bird eggs is more economical than using mammals. Studying the bird egg can provide insight into fetal effects independent of maternal parent influence. The egg is an object that can be placed in almost any desired position by the experimenter; it will remain there, a distinct advantage over free-ranging mammals. The shape of the egg represents a technical advantage over the mammal in that it is symmetrical externally, lending itself more easily to estimates of local and total absorption.

Theoretically, the bird egg gives no advantage to mammalian models in the study of teratogenic potential of RF radiation because concepts of organogenesis apply equally to avian fetuses and mammalian fetuses. To dismiss the considerable research on the teratologic effects of RF radiation in birds' eggs on the basis that the egg is poikilothermic whereas the mammal's egg is homeothermic would be an error. The mammalian conceptus is also poikilothermic; it has little, if any, control of its own temperature since it is entirely surrounded by placental fluids. It can remove itself of thermal energy only by radiating into surrounding maternal tissues because its capacity to rid itself of thermal energy is totally dependent on the gradient between itself and surrrounding tissues. If the mammalian conceptus' tissue temperature is increased because of RF-radiation absorption, it also must radiate that absorbed energy into its surroundings (dam), just as the egg in similar exposure conditions must radiate energy into the air of its incubator. If air or maternal temperatures are detrimentally high, then the loss of thermal energy from the egg or mammalian fetus is affected similarly.

Carpenter et al. (1960a) have studied RF radiation as an inducer of cataracts. These investigators have also likened the growth in the lens to the process of embryonic development and growth, where proliferation and differentiation take place concurrently. To further understand the RF-radiation-induced effects that appear in the lens, Carpenter *et al*. performed experiments using the egg of the domestic chicken. They irradiated almost 500 chick embryos at the 48-h stage and examined the eggs 48 h after irradiation, scoring incidences of survival and structural abnormalities. The irradiation was conducted in an anechoic chamber at 2450 MHz and at power densities of 200, 280, and 400 mW/cm^2. Estimates of SAR's for these power densities are 70, 98, and 140 W/kg, respectively (Durney *et al*. 1978). Power densities were determined by calorimetry using a saline-filled egg. The exposure durations ranged from 1 to 15 min. The eggs were incubated at 39 °C air temperature before, during, and after irradiation. At the 96th hour of development, all eggs were opened, and the embryos were removed, fixed, stained, and examined as whole-mounts.

Experimental results relevant to this section are presented in Table 3 of the Carpenter *et al*. 1960a publication. We have used the data in that table to calculate the relative summed incidences of dead and abnormal 96-h egg embryos for each experimental group (power density:time) and present the incidences in Figure 5-2.

The teratologic end points observed by Carpenter *et al*. (1960a) were death and abnormal morphology, which can be viewed as a continuum of one effect, interference with the normal processes of development. When abnormal structure is so severe as to interfere greatly with the continuation of development, the embryo cannot develop or maintain sufficiently normal structural and physiologic systems. The relationships between these systems collapse and the embryo dies. As stated earlier, indications of abnormal development increase in incidence and degree as the dosage increases. One mechanism for the increase in death is that, as the dosage increases, more embryos affect more changes in more systems, resulting in more deaths.

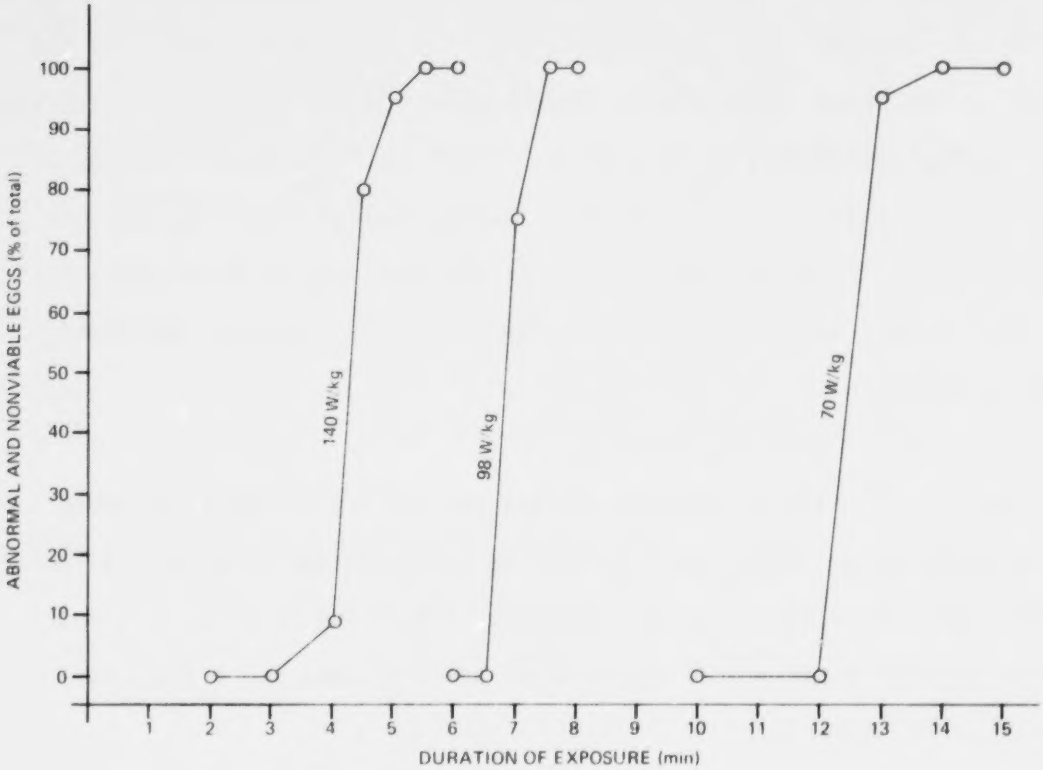

Figure 5-2. Summed incidence of abnormal and nonviable chick embryo eggs (percent of total) exposed to 2450-MHz radiation for varying durations at 70, 98, or 140 W/kg (Carpenter *et al*. 1960a).

Figure 5-2 contains three curves, one for each group of eggs exposed at dose rates of 140, 98, or 70 W/kg for varying durations. The data are plotted against the summed relative incidence of affected (dead or morphologically abnormal) eggs. The slopes of the curves are steep, indicating that small increases in the exposure duration caused disproportionate increases of effect. For example, the incidence in the group exposed for 10 min at 140 W/kg was 9 percent. An increase of only 30 s in exposure time caused a ninefold increase (80 percent) in incidence. An additional characteristic of these slopes is the disproportionate spacing along the exposure axis of the three curves.

Studies of RF radiation effects using the Japanese quail have been conducted exclusively by workers at the National Institute of Environmental Health Sciences. In their first attempt to induce terata in the quail egg, Hamrick and McRee (1975) exposed fertilized eggs in an anechoic chamber to 2450-MHz (CW) fields producing an SAR of 14 W/kg in the egg. The eggs were exposed for 24 h beginning 2 days after laying, then were returned to their incubators until 24 to 36 h after hatching. Several experimental replications occurred so that the sample numbers were 102 in the control group and 110 in the RF-irradiated group. After hatching, observations were made of cellular elements of blood and of selected organ weights. No significant differences between the two groups were seen in hatchability, blood cell parameters, body weights, or organ weights.

These authors also reported a similarly designed experiment on Japanese quail eggs, in which the eggs were exposed during the first 12 days of development at SAR's of 4.03 mW/g (McRee and Hamrick 1977). As before, the eggs were allowed to hatch and were then examined for teratologic alterations and blood-cell parameters. When the experiment was conducted at an environmental temperature of 35.5 °C, there were no significant changes in body weights, organ weights, or blood-cell parameters.

The authors also demonstrated the importance ambient temperature can play in experiments in which RF radiation is the toxic agent under investigation. Absorption of RF radiation energy produces increased temperature. In most studies of reproductive effects reviewed in this document, fields were at sufficiently high power densities to cause significant depositions of energy. Temperatures in the animal subjects were usually increased by 0.5 °C or more. Therefore, the ambient temperature in which the subject is maintained or treated can be a significant determinant of a resulting trend.

Levels of ambient temperature can be especially relevant to experimental subjects that do not have a significant thermoregulatory capability. For example, the report by McRee and Hamrick (1977) included the results of an experiment where Japanese quail eggs were in an environment at a temperature only slightly higher (+1.5 °C) than in the experiment discussed above (35.5 °C). The authors began their study using an ambient temperature of 37 °C because that is the temperature at which quail eggs are conventionally incubated. But this ambient temperature, with the addition of a 4 W/kg SAR, was sufficient to cause a 93 percent death rate of the fertilized eggs. The eggs that were irradiated at the same SAR, but at an ambient temperature lower by 1.5 °C, sustained only a 42 percent death rate. The results of this seemingly slight (1.5 °C) increase in incubation temperature during RF irradiation shows that for this poikilothermic model, the quail egg, the temperature at which the egg is maintained during experimentation is critical.

5.3.1.2 Mammalian Models--

Morphologic teratology--The mouse is commonly used in the laboratory for determining the teratogenic potential of toxic agents and also appears to be a useful model for determining the teratogenic potential of RF radiation. The mouse's size is conducive to this kind of experimentation because the apparent resonance of mice is 2450 MHz, a frequency at which irradiation equipment is commonly and economically available.

Rugh et al. (1974, 1975) conducted several experiments on the mouse at 2450 MHz using the experimental techniques from work on the teratology of ionizing radiation to explore teratologic effects of microwaves. The investigators used a waveguide exposure system in exposing individual pregnant CF1 mice. All mice were exposed once on the 8th day of pregnancy to CW fields at 2450 MHz for 2 to 5 min at a forward power that delivered a measured average energy dose ranging from 2.45 to 8 cal/g; there were no control or sham-irradiated mice in this study.

These and a few other authors have reported dose parameters in calories or Joules per gram, which we have converted to the SAR unit (W/kg) used in this document. Each of the texts of the two papers by Rugh et al. (1974, 1975) refers the reader to the other for more detailed methodology, but neither adequately describes exposure factors to convert accurately the dose values to dose rate (SAR). Our best solution was to convert to a range. The range of doses given by Rugh et al. is 10.3 to 33.5 J/g delivered over 2 to 5 min. The four possible combinations (Table 5-8) of two extremes of dose

TABLE 5-8. CONVERSION OF J/g TO W/kg*

Average Dose (J/g)	Exposure Duration (min)	SAR (W/kg)
10.3	5	34
10.3	2	85
33.5	5	112
33.5	2	280

*W/kg = J/g x 1000 ÷ seconds (from Rugh *et al*. 1974, 1975).

(10.3 and 33.5 J/g) and two extremes for exposure duration (2 and 5 min) result in SAR's ranging from 34 to 280 W/kg for this study. The most probable range of values is 85 W/kg (10.3 J/g for 2 min) to 112 W/kg (33.5 J/g for 5 min).

The authors clearly demonstrated the teratogenicity of RF radiation in mice, especially the potential for death and generation of anomalies. By determining the energy dose in each pregnant mouse, and because varying doses were absorbed during the 2 to 5 min of exposure, the effect observed in each litter could be assigned to a definite whole-body average dose. This is the strong point in the Rugh *et al*. studies.

Rugh *et al*. (1974, 1975) showed that resorption of fetuses is a characteristic of the levels of RF-radiation exposure. Resorptions appeared at a dose rate of approximately 85 W/kg. Both the incidence of resorptions within litters and the incidence of litters with resorptions increased as the average dose increased. Near the maximum dose (33.5 J/g, approximately 110 W/kg) almost all the litters were affected. Even at 25 J/g, there were litters with 100 percent resorption rates.

Anomalies "... were various, but the one used for this study, and which occurred most frequently, was exencephaly (brain hernia) ...." The report also included data on resorptions, dead, and stunted fetuses. In lieu of numerical data, the incidences of brain hernia (also termed encephalocele, exencephaly, or cranioschisis) are given by the authors in one figure. Data, as percentage of affected litters, were grouped into cells 8.4 J/g in width that ranged from 10.9 to 35.9 J/g. Approximately 30 percent of the litters given an average dose of 15 J/g (approximately 90 W/kg) had fetuses with brain hernias. Of those litters given an average dose of 31.8 J/g (estimated as 109 W/kg) almost all contained fetuses with some form of brain herniation.

Though sham, cage-control, or historical control value for the incidence of brain hernia in this mouse strain (CF1) is not given, the authors state "... since this aberration rarely if ever occurs without trauma, it is significant when even a single exencephaly occurs." However, one report of the incidence of spontaneous brain hernia in CF1 mice showed an occurrence of 11 exencephalic litters in a total of 90, approximately 12 percent of litters (Flynn 1968). Apparently, spontaneous incidences of anomalies are quite variable.

A report by Rugh and McManaway (1977) included data on mice exposed once for 4 min to 2450-MHz RF radiation (SAR = 100 to 114 W/kg) on days 0 to 11 (10 mice per day). In this group of mice (we cannot differentiate these data from those reported in Rugh et al. 1975 and Rugh 1976a,b) are uneven incidences of stunted fetuses (irradiated on day 4 of gestation) and death (irradiated on day 3, 8, or 10 of gestation). Rugh considers small fetuses as stunted and believes that this is a teratologic symptom.

Rugh's experiments included using a single, but high field intensity for a very short time (i.e., 4 min on the 8th day of gestation). A longer period (100 min daily during entire organogenesis) was used by Berman et al. (1978) in the exposure of pregnant CD1 mice to 2450-MHz CW fields at power densities of 0 to 28 mW/cm^2 in an anechoic chamber. Between 15 and 25 mice were irradiated simultaneously, each in a small ventilated container. Mean rectal temperature at the end of exposure to the highest power density (28 mW/cm^2) was 38.2 °C. SAR's were determined by twin-well calorimetry and averaged 2.0 W/kg at 3.4 mW/cm^2, 8.1 W/kg at approximately 14 mW/cm^2, and 22 W/kg at 28 mW/cm^2.

This study incorporated the examination of several variables of fetal response to toxic agents. Values were tabulated by power density for pregnancy rates, incidences of live and dead fetuses, live fetal weights, and incidences of anomalies. Values were expressed using the litter as the experimental unit. This is a conservative approach in experiments in which the potential fetal toxicity of an agent is determined (Atkinson 1975). Berman et al. (1978) also "corrected" the mean fetal weight of each litter by a factor representing the potential influence that litter size had upon fetal weight. This technique is also endorsed by Atkinson, because it allows greater confidence in the interpretation of data.

The study by Berman et al. (1978) demonstrated that daily exposure to 2450-MHz fields at intensities producing an SAR of 22 W/kg during the entire period of organogenesis caused a 10-percent decrease in body weight of mouse fetuses. The practical significance of this result is difficult to determine without experimental confirmation of the permanency or lack of reversibility of the smaller fetal weight. Until it can be shown that the effect is permanent (stunting) or temporary (delayed growth), the effect remains hygienically unresolved. The effect will have more practical significance if it can be shown that stunting is the result.

Berman et al. (1978) also reported on the incidences of anomalies. There did not appear to be a significant increase of individual or total anomalies at any SAR.

The C3H-HeJ strain of mouse was used by Chernovetz et al. (1975) in an attempt to determine the effects of fetal irradiation with 2450-MHz RF radiation. Pregnant mice were irradiated in a multimodal cavity for 10 min on the 11th, 12th, 13th, or 14th day of gestation at an SAR (determined by calorimetry) of 38 W/kg. The fetuses were examined near term (near the end of the gestation period) without any difference seen between the RF-irradiated and the sham-irradiated groups of fetuses. The variables observed in these fetuses related to the morphologic and the lethal aspects of the RF irradiation. Fetal body weights were not observed in these animals.

The scientific reports on the teratologic potential of RF radiation in the rat represent the major fraction of rodent work. The main reason for this, perhaps, is that many of the studies that have looked for morphologic changes have also included functional teratology as one of the end points. For that kind of study, especially behavioral studies, the rat appears to be preferred over the mouse.

Chernovetz is perhaps the most published author on the teratologic potential of microwaves in the rat. She reported (Chernovetz et al. 1977) the results of exposures of pregnant rats to 2450-MHz fields in a multimodal cavity (most likely the same device used to irradiate mice in experiments discussed above in Chernovetz et al. 1975) at an SAR calculated by calorimetry of approximately 31 W/kg. Exposures were conducted during 1 of 7 days, from the 10th through 16th day of gestation, and the fetuses were examined on the 19th day of gestation. Each single exposure lasted 20 min. The experiment included a total of 74 time-bred female rats, each assigned to 1 of 7 days of gestation and to 1 of 3 treatment groups (RF-irradiated, infrared-irradiated, or sham-irradiated). The result is an experimental design with 21 different cells into which 74 rats were distributed.

By the end of the 20-min exposure period, the mean rectal temperature in the surviving pregnant rats was 42 °C. Of the original group of 30 bred females that were used in the RF-irradiation group, 7 (or 23 percent) died, while none died in the sham-irradiated group. Therefore, the application of 2450-MHz RF radiation to bred rats for this duration at this SAR is lethal for a significant portion of the animals involved.

No numerical data on the gross teratologic consequences of this RF irradiation were given in the paper. However, comments were made in the text regarding the lack of any structural abnormalities. The number of resorptions was significantly higher (approximately 6 times) in the RF-irradiated than in the sham-irradiated fetuses, especially in the dams that had been irradiated on the 11th day of gestation. Fetal weights were also altered by the irradiation regimen; there was a small but statistically significant decrease in fetal weight. The alterations seen in the fetuses, in this case decreased fetal weights and death (in the form of resorptions), reflect the teratogenic potential of RF radiation exposure in the rat. It is important to remember that the fetal alterations were found from RF-radiation exposure regimens where rectal temperatures rose above 40 °C.

Chernovetz _et_ _al_. (1979) reported on the effect of 2450-MHz RF radiation in pregnant rats, this time at SAR's of 0, 14, or 28 W/kg. The same multimodal cavity was used, through which air at 22 ± 1.5 °C flowed at 0.75 m/s. Pairs of bred female rats were exposed for a 20-min period on the 8th, 10th, 12th, or 14th day of gestation and then were examined on the 18th day of gestation. With cage controls added to each of these cells, the complete experimental design used 4 different days of treatment and 4 treatments (cage control, 0 W/kg [shams], 14 W/kg, and 28 W/kg), and 6 bred females per cell, for a total of 72 bred females. Those rats irradiated at 28 W/kg developed rectal temperatures of approximately 42 °C, temperatures that were similar to the author's previous experiments in which bred female rats were dosed at 31 W/kg. The rats irradiated at 14 W/kg had a mean peak rectal temperature near 40 °C.

The values used by the authors in the statistical analyses were individual fetal values, not litter mean values. At the higher SAR level (28 W/kg), only ~ 10 percent below the sublethal level used in their previous report, the authors did not demonstrate lethality in the dams due to RF-radiation exposure. The 20-min exposure period at other levels of SAR produced no gross morphologic alterations in the fetuses or any severely edematous fetuses; there were also no statistically significant changes in resorption rates.

The results of fetal weights appear to be most interesting. In the previous study (Chernovetz et al. 1977), the authors reported that exposure for 20 min at approximately 31 W/kg on odd-numbered days of gestation produced a significant decrease in fetal weight. In the 1979 study, a similar result was also obtained from exposure at 14 W/kg on even-numbered days (12 and 14), or 28 W/kg on the 8th day of gestation. Unexpectedly, exposure at 28 W/kg on the 12th or 14th day produced an increased body weight. The unexpected increased body weight is an interesting observation, especially when it is viewed against the decreased fetal body weight documented in the same authors' previous paper and other reports of RF-radiation-induced fetal alterations in rats and mice.

Berman et al. (1981) were not able to elicit any fetotoxic or teratologic responses (body weight; numbers alive and dead; external, visceral, or skeletal morphology) in fetal rats irradiated daily (100 min/day) during gestation, even with a large number of litters. The dams were exposed to 2450-MHz radiation at power densitites of 0 or 28 mW/cm^2 (4.2 W/kg). These conditions caused a mean rectal temperature of 40.3 °C by the end of the 100-min exposure.

Kaplan (1982) did not find differences in the survival of squirrel monkeys up to 10 months of age after daily _in utero_ and postnatal exposures to 2450-MHz in multimodal cavities. Pregnant squirrel monkeys were irradiated for 3 h daily, beginning in the first trimester; after birth, the daily irradiation of the dams and their young were continued, and from 6 to 10 months of age only the young monkey was irradiated. The SAR was determined by calorimetry to be 3.4 W/kg. In 21 irradiated and 22 sham live-born, differences were not seen in sex ratio, the number dead by 10 months of age, or in the mean age at death. Postmortem examinations did not reveal any tendency to specific causes for death. The results of this study did not confirm the results of suspected increased lethality in squirrel monkeys from a previous study.

Functional teratology--Functional teratology is a field of reproductive toxicology that has allowed increasingly greater insight into the toxicology of environmental agents. The field contains a wide variety of specialists who examine the functional capacity of neonatal or growing animals after _in utero_ exposure.

The survival rate of fetuses can be used as an indicator of immediate effects on the fetus. The rate of survival of neonatal, infant, or older offspring can be also used as an indicator of delayed alterations in functional capacity long after insult during the fetal stage. For example, Kaplan et al. (1982) reported a study of the postnatal effects of in utero exposure (at dose rates to 3.4 W/kg) to 2.45-GHz RF radiation in squirrel monkeys. One effect the authors observed was an increase in neonatal deaths. However, a more intensive examination (Kaplan 1981) did not demonstrate any change in death rate and did not confirm the earlier study.

A simple test to determine whether RF irradiation in utero would alter the survival of mice after birth was conducted by Rugh (1976a). In this experiment, pregnant CF1 mice were exposed on the 9th, 12th, or 16th day of gestation to a regimen of approximately 4 min of irradiation at 2450 MHz, which resulted in a mean dose of ~ 25 J/g (104 W/kg). The survivors of this sublethal exposure were allowed to give birth and their young to mature to 2 months of age. At that time, the offspring were again irradiated in the same device until each one was dead. The time-to-kill and the mean dose-to-kill was determined as a measure of the radiosensitivity of the offspring irradiated originally as fetuses. At the time of death, the rectal temperatures of these mice ranged from 40 to 51 °C.

Because of body weight differences in the sexes at 2 months of age, the analyses were carried out by sex. Time-to-kill was shortened in males irradiated originally during the 12th or 16th day of gestation. The males irradiated originally on the 12th day of gestation had a lower mean dose-to-kill. Therefore, Rugh (1976a) has shown that irradiation by RF radiation on select days in utero can alter subsequent (and far removed in time) effects of re-irradiation with microwaves.

As noted, one effect observed commonly in fetuses exposed to RF radiation is decreased body weight. There are difficulties associated with interpreting altered fetal weight as an indicator of toxicity, especially when the permanency of decreased fetal weight (delayed growth vs. stunting) is not yet determined. But Rugh (1976a) gives evidence that mice irradiated as fetuses weigh less at 2 months of age. In that study, the mean weights of 2-month-old male offspring of dams irradiated during the 9th, 12th, or 16th day of gestation were all lower than concurrent sham-irradiated males ($P < 0.05$). Females irradiated during the 16th day of gestation were also smaller than their controls ($P < 0.05$), but not females from the 8th or 12th day groups. These results are evidence of a permanent change (stunting) in mice caused by RF irradiation.

Chernovetz _et_ _al_. (1975) carried out an experiment to observe alterations in functional capabilities after _in_ _utero_ irradiation. Pregnant mice were exposed once during the 14th day of gestation at an SAR of 38 W/kg, and the offspring were examined until weaning for survival. There were 15 dams each in the RF-irradiated and sham-irradiated groups. The statistical analyses, done by litters, show that there was a slight (approximately 12 percent) increase in the survival rate of the RF-irradiated litters as compared to the sham-irradiated controls.

Some experimental designs continue irradiation past birth. One example of chronic administration at 2450 MHz is reported by Smialowicz _et_ _al_. (1979a), where pregnant rats were irradiated daily for 4 h/day at a power density of

4 mW/cm^2 from the 6th day of gestation to term; irradiation of the offspring continued through 40 days of age. The SAR's were determined by twin-well calorimetry for several ages of the animals. Pregnant rats weighing 300 to 350 g had a mean SAR of 0.7 W/kg; offspring 1 to 5 days of age and 6 to 10 g in weight absorbed approximately 4.7 W/kg. There was no significant difference between the mean body weights of the males (female offspring were not used in this experiment) in the 12 sham-irradiated litters when compared to the mean body weights of the males in the 12 RF-irradiated litters.

Shore *et al*. (1977) reported decreased body weight and decreased brain weight in postnatal rats exposed *in utero* to 2450-MHz RF radiation. In this experiment, pregnant rats were exposed at an average power density of 10 mW/cm^2 (SAR estimated, from Durney *et al*. 1978, to be 2.2 W/kg) for 5 h per day repeatedly on days 3 through 19 of gestation. Rats were allowed to deliver naturally and were observed frequently thereafter. Rats were grouped by E- or H-field orientation during exposures, and only the 3-day-old offspring that had been exposed parallel to the E-field were significantly different, having lowered body and brain weights. We cannot easily explain this preferential decrement on the basis of either age or orientation during exposure. Our expectation is that there is no significant difference due to orientation in whole-body SAR in rats at this frequency (Gage *et al*. 1979).

In experiments conducted by Michaelson *et al*. (1978), some aspects of functional teratology of RF radiation were explored in Long-Evans rats. In these experiments, rats were exposed to 2450-MHz RF radiation at power densities of 10 mW/cm^2 for 1 h on the 9th and 16th day of gestation, or 40 mW/cm^2 for 2 h on the 9th, 13th, 16th, or 20th day of gestation. According to data based on water-calorimetry, an exposure at 40 mW/cm^2 produced an SAR of approximately 10 W/kg and approximately 2.5 W/kg at 10 mW/cm^2. Exposure at 40 mW/cm^2 caused an increase in the mean of rectal temperature of approximately 1 to 2 °C over that of the sham-exposed animals. The exposure at 10 mW/cm^2 (2.5 W/kg) on the 9th or 16th day of gestation caused a significant increase (approximately 0.5 to 1 °C) in the temperature of dams at the 16th day of gestation. There were no statistical differences in the sizes of born litters as a consequence of exposure during gestation. There also appeared to be no difference in the growth rates up to 21 days of age of the rat pups that were exposed to RF radiation as compared with shams, nor in their relative brain weights.

At the symposium where Michaelson described his work, Johnson *et al*. (1978) reported on a study, then in progress, on the functional teratologic effects in rats exposed to 918 MHz for 20 h per day for 19 days of gestation at a power density of 5 mW/cm^2. The experiment is especially interesting because it was conducted at a frequency close to the resonance of the experimental subject (rat), and it is the only reported study conducted with almost continuous exposure. The SAR in this study is approximately 2.5 W/kg, determined by calculations from thermographic scans. The eight RF-irradiated and eight sham-irradiated bred dams were maintained in the waveguide exposure apparatus under environmental conditions of 22 °C, 45 percent relative humidity, and *ad libitum* access to rat chow and water. The exposure was begun on the first day of pregnancy, the day on which the copulatory plug was first seen. In this experiment, the dams remained in individual waveguides or sham condition until day 20 of gestation, at which time they were removed and placed in delivery cages. At 4 days of age, the litters were culled to four males and four females per litter, which were then observed through 91 days of age.

There appeared to be no differences in the litter means for the number of pups born or for number dead during the first day after birth. There were no pups in any of these litters (including RF-irradiated, sham-irradiated, and cage-controls) with any visible physical defects. Body weights at birth, at 28 days of age, and at 91 days of age were analyzed for significant differences on an individual pup basis. The only statistically significant differences in body weights were found between the RF-irradiated and cage-control females at 28 days of age. A difference also existed in males at 91 days of age, when the RF-irradiated and the sham-irradiated males weighed less than the cage-control males.

Another parameter of development used as an assay of functional teratology in this study was the age at eye-opening. The phenomenon of eye-opening is a little understood but frequently used indicator of developmental maturation. There appeared to be a significant shift to earlier eye-opening in animals exposed to RF radiation during gestation, and this maturation was earlier by approximately 1 day.

Jensh reported a series of experiments designed to examine pre- and postnatally the effects of 915-MHz, 2450-MHz, and 6-GHz irradiation of rat fetuses (Jensh et al. 1979; Jensh 1979, 1980). These studies included irradiation up to 8 h daily during most of gestation with power densities not sufficient to cause increased core temperatures (915 MHz, 10 mW/cm^2, 2 W/kg; 2450 MHz, 20 mW/cm^2, 3 W/kg; 6 GHz, 35 mW/cm^2, 3.5 W/kg; SAR estimates from Durney et al. 1978, p. 96). Offspring were examined pre- and postpartum in a complex series of observations meant to locate behavioral or morphological alterations. None were noted.

In lieu of any other workable hypothesis supportable by experimental data, the most plausible available theory that can account for RF radiation effects is that, upon absorption, microwaves deposit energy that is converted to thermal energy. There remain differences between theories that attribute individual effects to a general input of energy, or the heating of local (hot-spot) areas, or some more subtle contribution of microwaves not characteristic of conventional methods of heating animals.

Comparisons between RF heating and infrared or convective heating have been conducted in the study of hyperthermia as a teratogenic agent. Edwards is a frequently cited investigator of the effects of hyperthermia on the development of mammals. His extensive work on this agent as a cause of congenital malformations is perhaps best summarized in one of his reviews (Edwards 1974), which describes his experiments on the teratologic manifestations of hyperthermia in the guinea pig. It should be noted that the guinea pig is an unusual laboratory animal in its long gestational development, approximately

65 days. During the latter two thirds of gestation in the guinea pig, the unborn offspring is in a stage of development similar to that which occurs after birth in the mouse and the rat. In itself, a long gestation period does not prevent use of the guinea pig as a model for teratogenesis. But the reader is forewarned that, when reading about teratologic experimental methodology, the administration of the agent at 40 or 50 days of gestational age in the guinea pig has no comparison in rodent fetuses and that this stage of development occurs postpartum in mice and rats.

Studies of the teratogenic potential of conventially induced hyperthermia in almost all the species used show some general changes that can be seen in RF-radiation-treated animals as well. The symptom of hyperthermia, whether induced by RF radiation or otherwise, causes varied anomalies (such as kinked tail, microphthalmia, exencephalia, cleft palate, general edema). This is evidence that hyperthermia is a general teratogen. Perhaps the only case where RF-radiation-induced and conventionally induced teratogenesis is not equal is in the development of smaller brain weights in fetuses heated by non-RF-radiation-heating agents. Except for Shore et al. (1977), perhaps the literature in RF-radiation-induced teratogenesis has not been sufficiently developed to show this effect of decreased brain weight.

Conventionally induced hyperthermia, like RF-radiation hyperthermia, appears to affect most species if sufficient energy is applied and proper timing of the agent is obtained. A sufficiency is usually manifested by a rise in maternal rectal temperature, usually over 40 °C, but often in a range of 41 to 43 or even 44 °C. At these temperatures, the teratogenic potential of heat applied by conventional means or by RF radiation does not appear to show any significant differences. The authors of one study attempted to differentiate teratogenic effects of microwaves from the more conventional methods of heating (in this case, infrared irradiation). Chernovetz et al. (1977) exposed pregnant rats to 2450-MHz fields at an SAR of approximately 31 W/kg, or to infrared radiation. The rectal temperatures of the RF-irradiated and the infrared-irradiated groups were similar (approximately 42 °C). The results of the exposures showed little difference in effects due to infrared heating or RF-radiation heating.

The symptom of decreased body weight of fetuses is a general developmental effect. This response to microwaves is commonly seen in experiments, even those experiments that have not otherwise demonstrated specific morphologic changes (e.g., O'Connor 1980). Body weight changes alone have also been seen in mice fetuses at temperatures < 40 °C (Berman et al. 1978).

Body temperatures reported in the above studies were those of the dam, usually measured in the dam's large intestine. Measurements of fetal temperatures after RF-irradiation have not been reported. A report by Morishima et al. (1975) provides some understanding of the physiologic changes that occur in the fetus as a result of conventionally induced hyperthermia. Morishima et al. used pregnant baboons and simultaneously monitored temperature and physiologic changes in the dam and the fetus during hyperthermia. The temperatures in these dams were raised to 41 to 42 °C by infrared lamps and warming pads. While the pregnant dam was maintained in an analgesic state using nitrous oxide inhalation anesthesia and intravenous succinylcholine chloride infusions, thermistors and catheters were placed at comparable positions in the dam and the fetus. Two groups of animals were used; one group was kept at 38 °C, and the temperature of the other was allowed to elevate gradually to 41 or 42 °C. At the more normal temperature, 38 °C, there was a slight but steady increase (0.5 °C) in the temperature of the fetus over that of the dam. When the temperature was increased to 40 °C in the dam, the fetal temperature rose accordingly and remained 0.75 °C higher than the dam's temperature. The hyperthermia produced increased uterine activity and some acidosis in the dam, and a profound acidosis and hypoxia in the fetus. If conditions comparable to those seen in the baboon are also seen in the mouse, then we might expect the mouse fetus to have temperatures greater than that of its dam.

That the teratogenic potential of RF radiation might be dependent only on the deposition of energy as heat was shown experimentally by Rugh and McManaway (1976). They exposed pregnant mice to highly teratogenic (high incidence of fetal death) levels of RF radiation with and without pentobarbital anesthetic. The mice exposed during anesthesia had normal rectal temperatures and normal incidences of fetal death. Therefore, the anesthetic protected against the primary temperature effect of the radiation by reducing "... the body temperature to a degree equivalent to the rise in temperature expected from the conditions used." This is clear evidence that the increased fetal abnormalities are strongly, if not solely, associated with increased maternal temperature.

Further evidence for a direct relationship between fetal effects and hyperthermia induced by RF radiation is shown in several reports (Dietzel and Kern 1970; Dietzel *et al*. 1972; Dietzel 1975). In these experiments, groups of pregnant rats were subjected to 27-MHz radiation to raise rectal temperature to 42 °C. From these data, the thresholds for malformation rates appear to be between core temperatures of 39.0 °C maintained for 5 min and 40.5 °C for 10 min.

Observed teratological effects are summarized in Table 5-9.

5.3.2 Reproductive Efficiency

This section discusses aspects of reproduction where the conceptus is not "insulted" directly by the agent, although the fetus may be involved in demonstrating the effect. Generally, reproductive efficiency is the capacity of the dam or sire to effect conception and to bear and rear offspring. Changes in this capacity might be due to alterations in behavior, physiology, or morphology. For example, reproduction efficiency might be affected by changes in maternal cyclical hormone secretions. Tests for reproductive efficiency are not conducted as frequently as those for teratologic effects, usually because the male and female reproductive systems require considerable alteration by a toxic agent to cause significant fetal wastage or increased reproductive efficiency. The testes as factors in reproductive efficiency are discussed separately in the next section.

TABLE 5-9. SUMMARY OF STUDIES CONCERNING TERATOLOGIC EFFECTS OF RF-RADIATION EXPOSURE

Effects	Species	Exposure Conditions*		
		Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)
30% survival of pupae	D. melanogaster		1 x 10	640
Embryonic LD_{50}	Chicken	200	1 x 12	70
		280	1 x 7	98
		400	1 x 4	140
Decreased postnatal survival	Mouse		1 x 4	104
Teratogenesis	Mouse		1 x 2-5	85-112
No change in teratogenesis	Mouse		1 x 10	38
Increased postnatal survival	Mouse		1 x 10	38
Maternal lethality, resorptions, decreased fetal weight	Rat		1 x 20	31
Decreased fetal weight	Mouse	28	12 x 100	22
No change post-hatching: hatchability, hemogram, body or organ weights	Japanese quail		1 x 1440	14
No change	Rat		1 x 20	14
No change	Rat	40	1 x 120	10
No change	Mouse	3.4-14	12 x 100	2-8
Teratogenesis	Mouse		12	4
No change	Rat	5	Many x 240	0.7-4.7
No change	Rat	28	12 x 100	4.2
No change	Squirrel monkey		Many x 180	3.4
No change	Rat	10-35	Many	1-3.5
No change	Rat	5	19 x 1200	2.5
Decreased body and brain weight	Rat	10	16 x 300	2.2

* Frequency used was 2450 MHz, except for Jensh (914, 2450, and 6000 MHz), and Johnson 1978 (918 MHz).

We have previously discussed the effects of 2450-MHz RF radiation on D. melanogaster reported by Pay et al. (1978). The fruit flies that were the subjects of that study were irradiated before production of ova. The SAR used in the study ranged from 400 to 800 W/kg. Reproductive efficiency, in this case the production of eggs, was significantly reduced in both conventionally heated and RF-irradiated females as compared with the shams. But, there appeared to be no significant difference in the production of ova from females exposed to RF radiation compared to those exposed to the conventional source of thermal energy.

The egg production of chickens can also be used to provide an index of reproductive efficiency or reproductive wastage. A single, intense exposure of day-old chicks was made in the experiment reported by Davidson et al. (1976). Described in one of four experiments is the reproductive efficiency of 28-week-old hens that had been irradiated as chicks on day 1 of age for 4.5 s at a power density of 800 W/cm^2 in a multimodal cavity. The estimated SAR was 2770 W/kg. No differences appeared between the control group and the irradiated group in the production of eggs during 100 days of laying. The authors also stated that a dose rate of 2500 W/kg for 9 s at 2450 MHz is a lethal dose in day-old chicks and that 42 percent of the chicks dosed for 6 s at 2810 W/kg died. The animals that survived were unconscious for up to 5 min. The day-old chicks had approximately the same sublethal SAR (2770 W/kg for 4.5 s) used in the examination for latent reproductive effects, but there were no deaths that could be directly attributed to the RF-radiation exposure.

From these experiments, it is concluded that the massive doses of this experimental regimen left no latent alterations in reproductive efficiency.

Rugh et al. (1975) reported an experiment in which they examined differences in average lethal dose of RF radiation (2450 MHz) during the estrous cycle of CF1 mice. The weights of the mice ranged from 29 to 31 g. There was a prior 20-min acclimation to the waveguide exposure chamber, and environmental conditions were 23.5 °C, 50 percent relative humidity, and an airflow of 38 L/min (0.38 km/h). There was a significant decrease in the average lethal dose for females in estrus as compared to the average lethal dose for those in diestrus ($P < 0.01$). The forward power was 8.24 W. This experiment shows that changes brought about during the reproductive cycle can affect radiosensitivity.

In summary, it appears that the efficiency of the female reproductive system is not easily altered. Only irradiation at extremely high dose rates has made changes in reproductive patterns. Small alterations from normal values, though detectable by modern scientific and statistical methodology, do not seem able to sway the general outcome of the reproductive cycle. Observed reproductive effects are summarized in Table 5-10.

TABLE 5-10. SUMMARY OF STUDIES CONCERNING REPRODUCTIVE EFFECTS OF RF-RADIATION EXPOSURE

Effects	Species	Exposure Conditions*		Reference
		Duration (days x min)	SAR (W/kg)	
Decreased ova production	*D. melanogaster*		400-800	Pay *et al*. (1978)
No change in egg production	Gallus	1 x 0.08	2770	Davidson *et al*. (1976)
Lethality changes with estrous cycle	Mouse			Rugh *et al*. (1975)

*Frequency was 2450 MHz in all cases.

5.3.3 Testes

Considerable scientific work has been done to determine effects of RF radiation on the testes. The testes are so placed anatomically that they can be conveniently irradiated without irradiating the remainder of the body. Tests for testicular function are also conducted easily. Quantitative changes in sperm concentration can be conveniently assessed using repeatable laboratory techniques. It is known that when the mammalian testes, which have a normal temperature of 33 to 35 °C, are heated to temperatures approaching abdominal temperature (37-38 °C) sterility can occur. Sterility consequent to high testicular temperatures can be viewed as a purposeful contraceptive agent or as an unintended toxic agent.

A report by Muraca _et_ _al_. (1976) describes the results of irradiation of rat testicles with 2450-MHz radiation. Each animal was anesthetized, placed in an anechoic chamber, then irradiated in a free field at a power density of 80 mW/cm^2. The SAR for adult rats was 16 W/kg (Durney _et_ _al_. 1978). But, the philosophical aim of this experiment was to examine the effects of RF radiation on the testes, and it may be appropriate to use the SAR of the testes alone as a more adequate expression of absorption. For that reason, we have also estimated (Durney _et_ _al_. 1978, Figure 41, model of a quail egg) that the average SAR to the testes might have been 60 W/kg.

In the experiment, the authors irradiated rat testes to produce increases of intratesticular temperature to 36, 38, 40, and 42 °C; the testes were then maintained at these temperatures. The technique of irradiation included implantation of a thermistor into one testis of the anesthetized male, with the temperature of that testis acting as the control of the on-off-on sequence of the RF irradiator. The authors irradiated both testicles, so that temperatures to which the testes were brought were within ±0.5 °C of the levels mentioned above. The duration of each irradiation at a power density of 80 mW/cm^2 varied from 10 to > 70 min. The animals were irradiated once or repeatedly during 5 consecutive days. Five days after the treatment ended, the animals were killed and their bodies were infused with solutions to preserve the testis that was not "invaded" by the thermistor. The microscopic appearance of the testicular tissue was categorized as follows: apparently normal; appearance of early inflammatory or degenerative changes in the spermatogenic epithelium without well developed necrosis; or severe degeneration of the majority of seminiferous tubules with coagulated cellular elements. This study also included a report comparing the effects of immersing the scrotum in a water bath.

When male rats were exposed once (80 mW/cm^2; 2450 MHz; 10 to 73 min; temperature of the testis maintained at 40 °C), there appeared to be no significant change in the incidence of apparently abnormal testicular tissue. After a single exposure of 10 min, during which the temperature of the testis was allowed to reach 42 °C, the number of animals that had some abnormal changes tripled. Multiple (five) exposures, even where the temperature reached only 36 °C for 60 min, caused all the testes to have some changes in the spermatogenic epithelium. When temperatures were allowed to reach 40 °C in the testes for repeated short periods (10 to 27 min, five times), severe degeneration in the spermatic tubules was seen in all the testicular samples.

This study points to two important factors of irradiation of the testes with 2450-MHz RF radiation: that a minimum temperature (> 40 °C) must be reached in an acute exposure, and that repetitive treatments are much more effective. These two factors interplay, as well, so that an acute temperature excursion, even as high as 40 °C for over 70 min, is not as deleterious as a lower temperature (36 °C) reached repeatedly (five times).

Fahim et al. (1975) conducted an experiment to compare the contraceptive capability of microwaves with that of other methods of heating. The authors used male Sprague-Dawley rats (Holtzman strain) and irradiated them with 2450-MHz radiation (from a diathermy unit of maximum output of 100 W) during pentobarbital anesthesia. The applicator of the diathermy unit was 7.5 cm from the testicles of the rat and provided near-field exposures that do not allow a good estimate of the associated SAR. By varying the power output of the unit and by varying the exposure time from 1 to 15 min, the authors developed four subgroups of animals: those in which testicular temperature reached 65 °C for 5 min, 45 °C for 15 min, or 39 °C for 1 or 5 min. The males were allowed to mate with normal females 24 h after treatment, and every 5 days thereafter until pregnancy was observed in the females. "The endpoint for fertility was the amount of time required for every surviving male in the treatment group to impregnate a female." Later, the sexual organs were weighed, and histological examinations were made of the testes and secondary sex organs.

Raising the temperature of the testes to 65 °C for 5 min or to 45 °C for 15 min caused complete infertility in the males for 10 months. When these testes were examined histologically, there was no observable spermatogenesis. When the temperature was raised to only 39 °C, 70 percent of the males retained normal breeding capability, whereas the remaining 30 percent recovered their fertility within 2 wk. Histological sections indicated normal spermatogenesis. There appeared to be no differences in testicular weights or secondary sex-organ weights, even in the group (45 °C, 15 min) that was sterile 10 months after the RF-radiation exposure had ended.

This experiment demonstrates that a temperature of 45 °C caused by RF-radiation exposure must be attained in the rat testes to produce permanent sterility. Temperatures that ranged to 39 °C, somewhat above rectal temperature, for only a short period (5 min) were not effective and produced only temporary, if any, infertility. Along with the permanent sterility induced by the high temperatures (minimum of 45 °C), there was damage to the tubules and a lack of spermatogenesis.

Sterility can occur in rats following RF-radiation exposure. At high temperatures, epithelial and tubular structures of the testes can be damaged permanently. At lower temperatures (approximately normal body temperature) for short durations, the temperature in the testicles due to RF-radiation exposure resulted in temporary sterility. This last condition implies that the spermatogenic cells themselves are not damaged permanently. The rat's spermatogenic cycle has a duration of about 10 wk, i.e., it takes about 70 days from the first meiotic divisions of sperm generation in the germinal epithelium until the time when the sperm are fully matured, in place, and ready for ejaculation. During the last 2 wk of spermatogenesis, sperm are located in the tubules of the testes and in the epididymis and require very little additional maturation. There is a constant stream of maturing sperm, because various seminiferous tubules are in different stages of this long cycle. The most mature stages of the spermatogenic cycle are most sensitive to heat (Van Demark and Free 1970). The permanent (10-month) sterility seen in the experiment above is due not only to loss of the most mature and most heat-sensitive stages, but also to the loss of sperm at all stages, including those stages involving the germinal epithelium. The 2-wk temporary infertility seen in the less affected males was caused by the loss of only the most mature and most heat-sensitive sperm.

A study to demonstrate an alteration in functional fertility was conducted by Berman et al. (1980). The authors' report concentrated on chronic exposures of rats to 2450-MHz radiation in an anechoic chamber. There were three separate experiments:

(1) Exposure at a power density of 5 mW/cm^2 for 4 h/day, daily, from the 6th day of gestation through 90 days of age postpartum;

(2) Exposure at a power density of 10 mW/cm^2 for 5 h/day for 5 days, beginning on the 90th day of age postpartum; and

(3) Exposure at 28 mW/cm^2 for 4 h/day, 5 days a week, for 4 continuous weeks, beginning on the 90th day of age postpartum.

The main purpose of the experiments was to evaluate potential mutagenic effects of RF radiation on the germ cells of the male rat. Male rats were bred to untreated female rats shortly after the end of the treatment period. No mutagenic effect was demonstrated. The breeding data of the assays used in these experiments were used to evaluate the effects on the spermatogenic function in rats.

In the first experiment, the animals were exposed daily from the 6th day of gestation to 90 days of age, at a power density of 5 mW/cm^2. In this experimental group, the SAR varied inversely with the growth of the animals, i.e., from approximately 4.5 W/kg in neonates to approximately 0.9 W/kg at 90 days of age. Twin-well calorimetry was not used in the other two experiments, and SAR's are estimated at 2 W/kg at a power density of 10 mW/cm^2, and 5.5 W/kg at 28 mW/cm^2.

In this study, temperatures of the testes of rats exposed up to 90 min to 2450-MHz fields at 28 mW/cm^2 showed an increase from a pre-exposure level of 34 °C to almost 38 °C after exposure. Simultaneously recorded rectal temperatures were ~ 3 °C higher than temperatures of the testes during the entire period. Sham-irradiated animals had testicular temperatures ranging from almost 32 °C to approximately 35 °C. The exposure at 28 mW/cm^2 during the 90-min period produced a temperature in the testis equivalent to the normal rectal temperature.

Chronic exposure at 5 mW/cm^2 from the 6th day of gestation through 90 days of age appeared to have no effect on the reproductive efficiency of the male rats when bred with normal females. Also, exposure at a power density of 10 mW/cm^2 (SAR ~ 2 W/kg) at 90 days of age for a period of 5 days had no effect on the reproductive efficiency of the males. It was only the most severe regimen, the exposure of adult male rats at 28 mW/cm^2 for ~ 4 wk (estimated SAR ∿ 5.5 W/kg), that caused any alteration in reproductive function. This exposure produced a severe decrease in the reproductive ability of the males; only 50 percent of the females that were available to the males for breeding became pregnant during the week immediately following the exposure period. The breeding returned to normal beginning at the 3rd week after irradiation (the next period of test breeding). The animals bred normally thereafter. No examination was made of the testes of animals exposed at 28 mW/cm^2. The temperatures reached in the testes at the highest power density (28 mW/cm^2) were similar to those reported by Fahim _et al_. (1975) where histological changes were seen.

Cairnie et al. (1980) studied the effects in mouse testes after a range of whole-body exposures of up to 30 days for 16 h/day at 2450-MHz and power densities up to 36 mW/cm^2 (average whole-body SAR = 7 W/kg; average testicular SAR = 14 W/kg). These exposures caused no measurable increase in testicular temperature. No changes were seen in the number of dead testicular cells, the number of epididymal sperm, or in the percentage of abnormal sperm after exposure, even up to 8 wk after exposure. Four strains of mice were used, and no strain susceptibility was observed.

Varma and Traboulay (1975) were able to cause severe scrotal and testicular burns in anesthetized mice after exposure for 20 min to 1.7 GHz and 200 mW/cm^2 (whole-body SAR estimated at 80 W/kg). Exposures of < 100 min to 10 mW/cm^2 at this frequency caused little or no damage. But a 100-min exposure caused general testicular damage without changing Sertoli and interstitial cells. No severe changes occurred at 3 GHz, 50 mW/cm^2, for 20 min (SAR = 20 W/kg).

In the studies reported by Ely et al. (1964), 2880-MHz radiation was used to irradiate only the testicular area in groups of dogs. The animals were anesthetized during exposures while temperatures were measured in the testis. Irradiation of the testicular area continued until a peak temperature was reached; the RF radiation was then turned off manually so that the testes could cool, at which point the RF radiation was turned on once again. This cycling of exposure was completed many times so that the animal's testes could be kept at a "steady" temperature for a considerable length of time. The normal temperature of the testes of the dogs was ~ 33 °C, 5 °C lower than that of the rectum.

According to this report, exposure of the testes at 20 mW/cm^2 caused an elevated testicular temperature of 36 °C at 33 mW/cm^2, 38 °C at 45 mW/cm^2 and up to 40 °C. As 38 °C is the approximate body temperature in the dog, bringing the testes to body temperature can expect to produce sterility if the elevation is sufficiently chronic. It appears then, that 45 mW/cm^2 is required to produce this type of effect.

There is a large body of literature on the fertility effects caused by temperature increases, such as when the testicles are clothed to prevent the normal thermal radiation. Even high environmental temperatures, when sustained, can produce infertility in male rats. One example of this is a report (Pucak et al. 1977) describing deaths in a large rat-production colony in which room temperatures accidentally reached as high as 31.6 °C for 2 days and as high as 37.7 °C in individual cages. Under these conditions, approximately 3,000 of 14,000 Sprague-Dawley rats died from heat prostration. When examined 18 days after the incident, 25 percent of the surviving males showed bilateral atrophy of the testicles, which were approximately half the normal size. Histological examination showed atrophy of the spermatic tubules and failure of spermatogenesis. The proportion of affected testicles ranged from 50 to 75 percent. Five weeks after the incident the animals with small testes were still sterile. In comparison with the temperatures seen in this study, raising the temperatures of testes to 42 °C by RF-radiation exposure appears to be an extreme experimental regimen. Observed testes effects are summarized in Table 5-11.

TABLE 5-11. SUMMARY OF STUDIES CONCERNING REPRODUCTIVE EFFECTS OF RF-RADIATION EXPOSURE IN THE RAT

	Exposure Conditions*			
Effects	Intensity	Duration (days x min)	SAR (W/kg)	Reference
Spermatogenic tissue abnormal	80	1 x 10-73 5 x 10-73	16 16	Muraca et al. (1976)
No change	5	many x 240	0.9-4.5	Berman et al. (1980)
No change	10	5 x 360	2	
Temporary sterility	28	20 x 240	5.5	

*Frequency was 2450 MHz in all cases.

5.3.4 Unresolved Questions

5.3.4.1 Teratology--

A threshold of teratogenic effects due to RF radiation has not been determined. The measurement of threshold will have to include the entire range of teratogenic effects: lethality, anomaly production, decreased body weight in fetuses, and alteration of postnatal function. Even at this stage of development of the data relating to RF-radiation-induced teratogenesis, a picture is appearing in which the degree of response is dependent on the level of whole-body SAR, the duration of exposure, the timeliness of the exposure, and the species, all of which complicate the threshold determination. It is not yet clear if threshold can be based on a finite whole-body SAR for all species or is some adjustment or proportion will be necessary for species size, metabolic rate, thermoregulatory capacity, etc. So far, the only physiologic variable that can be supportably associated with teratogenic effects is the colonic temperature of the dam during or at the end of exposure. The mouse and rat, two extensively studied species, show a minimum temperature of approximately 40 °C in the dam is associated with teratologic symptoms. However, whole-body SAR's required to cause temperature excursions like this are much higher in the mouse than in the rat. Therefore, an adequate relationship of teratogenesis to SAR alone is not apparent. The maternal colonic temperature, then, is the only available indicator of a threshold for teratogenesis in mammals.

Published reports that meet the criteria for consideration in this document have limited their examination of the fetal results of gestational exposure to a gross morphological change or one that might be seen under low magnification (15X). There has been no organized attempt to examine in histologic detail fetuses that have been irradiated _in_ _utero_. Authors of one study (McRee _et_ _al_. 1980b), however, made a detailed examination of embryonic hearts but could not demonstrate changes in morphologic, ultrastructural, or enzymatic activity. The subjects were Japanese quail which had been exposed daily for 8 days to 2450-MHz radiation at SAR's of 4 and 16 W/kg.

There are classifications of fetal changes that represent no gross structural deficit, but nevertheless represent some variation of structure. An example of a variation that may not be considered by all teratologists as a "deficit" is a small but normal fetus. However, if the incidence of this variation is consistently increased because of the application of a toxic agent, it could be considered an expression of embryotoxicity. The decreased body weight so often seen in offspring exposed to RF radiation (Berman et al. 1978; Chernovetz et al. 1977, 1979; Rugh 1976a) might otherwise be considered as a lesser category of "structural variation without deficit" were it not that decreased weight is so consistent in these experiments. Whether this decreased fetal weight is temporary (i.e., only a delayed growth that will disappear in the neonatal stage) or permanent (i.e., a stunting of the fetus that will persist) has not yet been scientifically resolved.

There is one aspect of the literature on the teratogenic potential of RF radiation that deserves further discussion. More than half the papers in this document on teratogenesis report experiments with the rat. Chernovetz et al. (1977) raise an interesting point about using the rat in determining the teratogenic potential of RF radiation. The authors argue that because levels of microwave exposure which are associated with high mortality rates of dams do not also produce fetal structural abnormalities in the rat, "... that the teratogenic threshold of microwave radiation is higher than the dam's threshold of mortality," and hence "... that maternal mortality is more probable than malformation of the fetus, irrespective of the dose."

The problem of using animal models in determining teratogenic potential in humans is that there is no assurance that any of these models is a real estimate of effects in humans. The concepts supporting the use of animals as models of human beings require that the response be demonstrated in a number of species, so that the resultant generality can be more confidently extended to humans. Therefore, we seek among species some generality of effects of microwaves on the fetus. Mice and rats are the two laboratory animals upon which rest almost all of the data of RF-radiation-induced teratogenesis. Any difference between the two species in their teratogenic response to RF radiation, therefore, becomes important.

5.3.4.2 Reproductive Efficiency and Testes--

The testes contain, besides sperm-producing tissues, interstitial cells that secrete testosterone, the male hormone. Gunn _et al_. (1961) described the effect of 24-GHz radiation on the morphology and function of the interstitial cells in rats. They exposed rats once at this frequency for a period of 5 min at a power density of 250 mW/cm^2, which caused the temperature to rise to 41 °C in the testes. As a result, there were scrotal burns, severe edema, and spermatic tubular degeneration, but no interstitial-cell pathology.

The testosterone secreted by the interstitial cells of the testes regulates zinc uptake by the dorsolateral prostate. When Gunn examined zinc uptake in RF-irradiated rats that had no interstitial cell pathology, he found a decreased uptake. Gunn related the decreased function of this secondary sex organ to decreased testosterone secretion.

The effects seen by Gunn were produced at a frequency of 24 GHz. This is such a short wavelength that, theoretically, there would not be any significant penetration to affect the dorsolateral prostate directly. The tests using the dorsolateral prostate as an indicator of sexual function in the rat have been commonly used by Gunn and others in other types of experimental situations.

It is not known why and how the dorsolateral prostate lost its capacity to function normally when there was no observable change in the interstitial tissues, the other testicular damage appeared to be minimal, and the energy could not reach the prostate. This appears to deserve additional scientific attention and exploration.

The literature we have cited does not lend itself to extrapolation of effects of RF radiation that cause only small increases in the temperature of the testes. The lack of data on RF-radiation effects at lower power densities (which cause lower testicular elevations of temperature than have been cited in the articles above) is especially important in light of suggestions that thermal energy, in the form of absorbed RF radiation, can be used as a contraceptive in men (Medical World News 1974; Arehart-Treichel 1974).

One report by Rugh (1976a) contains data on survival in RF-radiation fields that are different in males and females. In this study, mice of both sexes and of three ages (weanlings, young mature, and aged) were irradiated with 2450-MHz RF radiation until dead. Of the three variables (age, sex, body weight) examined for their contribution to RF-radiation lethality, Rugh found that "The overall conclusion would be that no matter at what age ... absorbed dose to death ... is different for the two sexes. Females are slightly more radiosensitive ...." These results are not explained easily. Although they are not apparently related to sexual function, they were included here on the basis of sexual differences.

5.4 NERVOUS SYSTEM

Ernest N. Albert

The nervous system in higher forms of life is the result of an evolutionary development in response to the environment, and has reached a very high stage of development in man. The body experiences many environmental stimuli and responds to these conditions either voluntarily or involuntarily. These responses are mediated by the nervous system.

Briefly, specialized receptors enable the human being to perceive visual, auditory, thermal, mechanical, chemical, electrical, pain, and pressure stimuli, and send the sensory information to the central nervous system (CNS, i.e., brain and spinal cord) via the peripheral nervous system (PNS). In addition, the brain is the site of mental operations such as mathematical integration, thought, memory, will, anger, and love. The brain integrates all of the sensory information and provides a response appropriate to maintaining homeostasis within the entire organism.

These functions of the nervous system are carried out by its two major divisions: (1) the somatic or voluntary, and (2) the autonomic or involuntary. The somatic or voluntary division is primarily involved in controlling conscious activities. On the other hand, the autonomic or involuntary division of the nervous system is more involved with those functions of the body that an individual cannot control (e.g., regulation of blood pressure and heart rate). When the body is suddenly stressed, the heart begins to beat faster; respiration rate and blood pressure increase involuntarily.

The basic structural units of all parts of the nervous system consist of cells (neurons and glia) and their processes (axons, dendrites, and terminals). There are many types of neurons and glial cells as well as many modifications of their axons and dendrites. These cells and their processes communicate with each other, as well as with muscles and glands of the body, via chemical and electrical means in integrating information and maintaining homeostasis.

When an environmental condition fluctuates within acceptable limits, the nervous system responds by compensating within the body's physiological limits with no apparent harm. However, extreme environmental conditions stress the nervous system beyond these limits, resulting in abnormal physiological functions. Such abnormal functioning could result from exposure to RF radiation. Therefore, it is important to investigate and evaluate the interactions and thresholds of interactions between RF radiation and the nervous system.

A critical review of the literature in this area permits the following general statements to be made about the effects of RF radiation:

(a) Morphology. There is ample evidence that acute and chronic exposure of animals at sufficiently high intensities of RF radiation (CW or PW) produces morphological alterations in the nervous system. The morphological changes are qualitatively similar after acute and chronic exposure (at high and low densities), but quantitatively there are greater alterations in neuronal structure at higher (> 10 mW/cm^2) power densities and after chronic exposures. In general, PW radiation produces greater changes than CW radiation. Almost all reported changes due to RF-radiation exposure are reversible.

(b) Blood-brain barrier (BBB). There is an ongoing controversy whether RF radiation at low power densities alters the BBB of experimental animals. At present, no definitive conclusions are possible concerning RF-radiation effects on the BBB at low power densities (< 10 mW/cm^2).

(c) Pharmacologic effects on CNS. PW radiation appears to have a potentiating effect on drugs that affect nervous system function. Whether RF radiation also has an inhibiting effect on neuropharmacologic drugs is not certain.

(d) Effect on neurotransmitters. There are no data on this subject at low power densities (< 10 mW/cm^2). However, at high power densities and SAR's (> 24 W/kg) there appears to be an effect on the release of neurotransmitters after exposure. Whether there is an increased or a decreased release depends on the specific neurotransmitter.

5.4.1 Morphologic Observations

The nature of morphologic changes in the nervous system of exposed animals depends on the frequency, power density, duration, and modulation characteristics (e.g., PW or CW) of the radiation. Gordon (1970) and Tolgskaya and Gordon (1973) report that severe damage to the brain occurs when RF radiation of various frequencies at high power densities (> 40 mW/cm^2), producing measurable ΔT's, is used. These changes consist of hemorrhages, edema, and vacuolation of neurons after a 40-min exposure to 3000- or 10,000-MHz PW or CW radiation at 40 to 100 mW/cm^2. At 20 mW/cm^2 similar but less severe effects were observed. Further, 3000-MHz radiation produced more marked changes than 10,000 MHz of equal power density. However, Austin and Horvath (1954) did not observe similar changes in brains of rats that became convulsive and hyperthermic (brain temperature ~ 43 °C) due to a single exposure to 2450-MHz radiation. These authors observed only mild pyknosis and hyperemia in some areas of the brain. Albert and DeSantis (1975, 1976) did not observe hemorrhage, gliosis, or focal necrosis in Chinese hamsters exposed to 2450-MHz (CW) radiation at 50 mW/cm^2 (SAR estimated at 17.5 W/kg) for 30 to 120 min, but they did observe swollen neurons with frothy cytoplasm in the hypothalamic and thalamic regions of the brain. Such observations were not seen in the cerebellum, pons, or spinal cord. Histologic change in the brains of rats have also been reported at low power densities ($<$ 10 mW/cm^2) of 3000-MHz microwaves after multiple 30-min exposures. The histological alterations include cytoplasmic vacuolation of neurons, axonal swelling and beading, and swelling in and decreased numbers of dendritic spines (Tolgskaya and Gordon 1973; Albert and DeSantis 1975; Gordon 1970). All of the above-mentioned changes were reversible after 3 to 4 weeks. Baranski (1972b) noted that exposure of guinea pigs and rabbits to 3000-MHz (PW and CW) radiation at power densities of 3.5 to 25 mW/cm^2 (SAR estimated at 0.4 to 2.5 W/kg) resulted in myelin degeneration and metabolic alterations in glial cells.

Qualitatively, the morphological effects on the CNS are similar at 10 to 50 mW/cm^2 power densities, but quantitatively they are greater at higher power densities. Most scientists agree that irradiation at these power densities can raise the body temperature. Soviet scientists have reported similar morphological changes at 1 mW/cm^2 after chronic irradiation, and they do not consider these alterations at 1 mW/cm^2 of thermogenic origin. Tolgskaya and Gordon (1973), Baranski (1972b), and Baranski and Edelwejn (1968) further state that morphological effects are more marked after PW or chronic exposure than after CW or acute exposure. Most Eastern European studies claim full recovery by irradiated animals in 1 to 3 weeks after exposure at less than 10 mW/cm^2. Albert and DeSantis (1975, 1976) found continued existence of neuronal cytopathology in animals 2 weeks after exposure. Perhaps a longer recovery period in the latter study would have shown complete reversibility.

Switzer and Mitchell (1977) described the existence of myelin figures in brain dendrites of rats exposed to 2450-MHz (CW) fields for 550 h over a 110-day period (average SAR = 2.3 W/kg) and allowed 6 weeks for recovery. These authors did not observe any gliosis, perivascular edema, or synaptic pathology. However, irradiated rats in this study exhibited marked disruption of discriminative performances during exposure.

Takashima _et_ _al_. (1979) exposed male rabbits to 1- to 30-MHz fields amplitude modulated at ~ 15 Hz or 60 Hz during 2- to 3-h single exposures or during 4 to 6 weeks of chronic exposure. The electric field strengths ranged from 60 to 500 V_{rms}/m. Acute and chronic EEG recordings were obtained from animals under sodium pentobarbital anesthesia. There was no temperature rise in the exposed animals. The EEG recordings after acute exposures at field strengths of 60 to 500 V_{rms}/m or after chronic exposures at strengths up to 70 V_{rms}/m showed no differences between control and experimental animals. However, chronic irradiation at higher field strengths was associated with abnormal patterns. These consisted of bursts of high amplitude spindles at 90 V_{rms}/m as well as suppression of activity at 500 V_{rms}/m. All brain activities returned to normal a few hours after irradiation. The results in this study appear to be free of electrode artifacts because chronic exposures were made without electrodes, and all recordings were made when the fields were switched off. The effects of anesthesia are not clear, and the natural fluctuations of brain activity also complicate interpretation of the results.

Although the occurrence of high-amplitude spindles in irradiated animals in this study is similar to that described by Bawin et al. (1973), it is difficult to compare the two results because, in the latter study, chronically implanted electrodes may have interfered with the imposed fields. Takashima et al. (1979) confirmed the existence of artifacts during irradiation when implanted electrodes were used.

We can conclude that RF radiation of centimeter wavelengths causes morphological changes in the CNS of experimental animals following acute or chronic exposures at low power densities (< 10 mW/cm^2). Note that, in most of the low-exposure studies, total recovery was observed after 3 to 4 weeks.

5.4.2 Blood-Brain Barrier Studies

In the past few years, contradictory reports have been published concerning the effects of RF radiation on the permeability of the BBB. (For reviews, see Albert 1979a and Justesen 1980.) Some of these reports indicate that direct RF-radiation effects in experimental animals might result in increased permeability of the BBB (Frey et al. 1975; Oscar and Hawkins 1977; Albert and DeSantis 1976; Albert 1979b). Other reports indicate that increased permeability might be mediated by hyperthermia induced by intense RF fields (Sutton and Carroll 1979; Merritt et al. 1978; Lin and Lin 1980). Preston et al. (1979) and Preston and Préfontaine (1980) reported negative findings at lower power densities. Some of these discrepancies may be attributed to differences in techniques employed to assess changes of permeability. These methodologies consist of gross examination of brain slices, single-passage isotopic tracers, fluorometric measurements, and electron microscopic tracers. All of these techniques have some inherent shortcomings, either in quantitation or sensitivity. Thus, unless the changes of permeability are diffuse and significant, positive results may not be readily apparent. Further complications are reports that average power density, peak power, and pulse width may be important parameters affecting the BBB permeability (Frey et al. 1975, Oscar and Hawkins 1977). Therefore, one must consider the limitations of the techniques and the exposure parameters before reaching conclusions regarding effects of RF-radiation on the BBB.

Frey et al. (1975) were the first authors in the United States to report a permeability increase in the BBB of the rat after RF-radiation exposure. They observed that a 30-min 1200-MHz exposure (CW) at 2.4 mW/cm^2 (SAR estimated at 1.0 W/kg) resulted in a statistically significant increase in fluorescein in brain slices of experimental animals over controls. Most of the fluorescein appeared to be concentrated in the vicinity of the lateral and third ventricles. Some dye also was detected in the metencephalon. These authors also reported similar but heightened alterations in the permeability of the BBB when rats were irradiated with PW radiation at 2.1 mW/cm^2 peak and 0.2 mW/cm^2 average power density (SAR estimated at 0.8 W/kg). Their results also indicated that PW radiation was more effective in altering brain permeability than CW--once again, the theme of PW radiation producing greater biological effects than CW surfaces in these studies.

Merritt et al. (1978) were unable to replicate the fluorescein studies of Frey et al. (1975). However, increased brain permeation of fluorescein-albumin (mol. wt. 60,000) was produced in rats heated to 40 °C by hot air or by RF radiation. They concluded that hyperthermia per se, and not field-specific effects of RF radiation, is the essential determinant of increased permeability. Using sodium fluorescein and Evan's blue, Lin and Lin (1980) also found no change in BBB permeation after a single 20-min focal exposure within the rat head at 0.5 to 1000 mW/cm^2 (local SAR's ranged from 0.04 to 80 W/kg) at 2450 MHz (PW). Albert (1977, 1979b) and Albert and Kerns (1981), using electron microscopic tracer methodology, followed the movement of horseradish peroxidase (mol. wt. 40,000) in rat and Chinese hamster brains after 2450-MHz (CW) irradiation in the far field at 10 mW/cm^2 (SAR estimated at 0.9 to 2.0 W/kg). The authors reported focal areas of increased permeability in brains of 35 percent of the irradiated animals in contrast with 10 percent in controls. Areas with increased permeability were seen with greater frequency in the thalamus, hypothalamus, medulla, and cerebellum than in the cortex or hippocampus. Using the same parameters of exposure and species as above, Albert (1979b) and Albert and Kerns (1981) showed that within 2 to 4 h after irradiation, there was no evidence of increased BBB permeability, thus demonstrating complete reversibility of the RF-radiation effect. It was also shown that the increased permeability of the BBB appeared to be due to increased pinocytotic transport of the tracer rather than to opening of the endothelial tight junctions (Albert and Kerns 1981).

Sutton and Carroll (1979) observed increased permeability of the BBB to horseradish peroxidase when brain temperatures of rats were elevated to 40 to 45 °C for a few minutes by 2450-MHz (CW) microwaves. A significant observation was that the integrity of the BBB and survival times at 45 °C (cerebral temperature) could be prolonged if core temperature was maintained at 30 °C. They hypothesized that perfusion of vessels with cool blood had a protective effect. This study indicates that severe hyperthermia induced by RF radiation might result in increased permeability of tracer proteins in rat brains.

In a physiological study using radioisotope tracers, Oscar and Hawkins (1977) exposed rats to 1.3-GHz (CW or PW) radiation for 20 min. Using the technique of Oldendorf (1970), they found after CW irradiation at 1 mW/cm^2 (SAR estimated at 0.4 W/kg) that there was a significantly greater uptake of mannitol (mol. wt. 182) and inulin (mol. wt. 5000), but not dextran (mol. wt. 60,000), in brains of exposed animals. Similar, but greater, uptake of these compounds was observed after PW irradiation (average power density 0.3 mW/cm^2; SAR estimated at 0.1 W/kg) than after CW irradiation. Uptake of mannitol by the brain was quite dependent upon power density, pulse width, and number of pulses per second. Merritt et al. (1978), who also used the Oldendorf technique, reported that there was no significant change in uptake of mannitol or inulin in rats exposed to RF radiation under conditions similar to those used by Oscar and Hawkins (1977).

Preston et al. (1979), who also used the Oldendorf technique, exposed rats to 2450-MHz (CW) fields for 30 min at 0.1 to 30 mW/cm^2 (SAR estimated at 0.02 to 6 W/kg); no change in uptake of mannitol in the brain was found. They also speculated that the changes reported by Oscar and Hawkins (1977) may have been due to changes in blood flow. Later, Oscar et al. (1981) measured the blood flow in several brain regions during exposure to 2800-MHz (PW) fields at 15 mW/cm^2 (average) for 5 to 60 min and found increased local blood flow. They then suggested that previously reported BBB-permeability changes (Oscar and Hawkins 1977) may be less in magnitude than originally indicated.

A recent report by Preston and Préfontaine (1980) described studies on BBB permeability in rats exposed to 2450-MHz (CW) radiation both in the near and the far field. The far-field exposure took place in an anechoic chamber at 1 or 10 mW/cm^2 (SAR estimated at 0.2 to 2.0 W/kg) for 30 min. In the second study, a microwave applicator was placed on the rat head for a near-field exposure. The exposure consisted of a single 25-min irradiation (SAR's at 0.08 to 1.6 W/kg). In this second study the exposure took place after the tracer ^{14}C-sucrose was injected into the animal so that BBB function during irradiation could be examined. No change in permeation was found in either study.

5.4.3 Pharmacological Effects

RF radiation has been reported to alter effects of drugs that influence CNS functions. Baranski and Edelwejn (1968) noted altered EEG tracings and decreased tolerance to Cardiasol, a CNS stimulant, in persons working in microwave fields. To better understand their observations of humans, they conducted animal experiments. In their investigations on rabbits, these authors found that administration of Phenactil, a depressant of cortical activity, followed by 3000-MHz (PW) irradiation at 20 mW/cm^2 (SAR estimated at 3.0 W/kg) for 20 min, resulted in desynchronization of the EEG; i.e., the synchronizing of the EEG by Phenactil was reversed by irradiation, which indicates a stimulatory effect by microwaves on the brain-stem reticular formation. Under the same exposure conditions, these authors demonstrated that half the dosage of Cardiasol was required to obtain the same EEG reaction that was observed in control animals without previous irradiation; the authors concluded that microwaves potentiate the effects of Cardiasol. Chronic exposure of rabbits to 3000-MHz (PW) radiation at 7 mW/cm^2 (SAR estimated at 1.0 W/kg), 3 h/day for a total of 70 to 80 h resulted in violent convulsions after injection of the same dose of Cardiasol (3 mg/kg) as in controls, thus indicating that tolerance to Cardiasol was decidedly lower in chronically exposed animals than in controls. Chronic exposure also resulted in desynchronization and high-amplitude recording potentials in the EEG. In this study, thermal effects of microwaves were considered unlikely, and the authors suggested that microwaves may exert a stimulating effect on specific areas of the CNS. It should be noted that the EEG records were obtained with screw electrodes implanted into the skull of the rabbit and that the pulse modulation characteristics were not specified.

Servantie _et_ _al_. (1973) investigated the combined effects of microwave radiation and Pentetrazol, a convulsant drug. Mice were subjected to 3000-MHz (PW) radiation (maximum peak power = 600 kW and maximum mean power = 350 W), presumably for a few minutes per day for 8, 15, 20, 27, and 36 days. The mean power density measured in the absence of the animal was 5 mW/cm^2. At the end of exposure, 50 mg/kg of Pentetrazol was administered intraperitoneally. They observed that RF radiation affected the convulsive time and mortality rate. Specifically, they noted that there was no difference between controls and experimental animals through 8 days of exposure. After 15 days of irradiation, the animals exhibited delayed appearance of convulsions and were less susceptible to the epileptogenic action of Pentetrazol. However, after 27 to 36 days of exposure, the effect was reversed. The results indicate a biphasic response of mice over 36 days. Decreased incidence of mortality was observed in drug-injected animals if they were irradiated more than 8 days. Servantie *et al*. (1973) also investigated the effect of curare-like drugs on *in vivo* and *in vitro* preparations of the rat's sciatic nerve. They found that irradiated rats were less susceptible to paralyzing drugs. Similar findings were noted in sciatic-nerve preparations from rats. In addition, sciatic nerves isolated from irradiated rats were paralyzed to a lesser extent and recovered sooner than those of control rats. Servantie *et al*. (1973) suggested that, based on their observations, the effect of microwaves is more likely at the neuromuscular junction (synapse) and less likely due to secondary effects on the metabolism or binding of the drugs.

Goldstein and Sisko (1974) investigated the effects of pentobarbital and 9.3-GHz (CW) microwaves at a power density of 0.7 to 2.8 mW/cm^2 (SAR estimated at 0.1 to 0.3 W/kg) on the behavior and EEG patterns of rabbits. They reported that there was no difference in EEG patterns between control (pentobarbital-injected) rabbits and rabbits treated with pentobarbital plus RF irradiation (0.7 mW/cm^2) during the the first 5 min. However, after a latent period, cycles of intense arousal and sedation accompanied by other behavioral changes occurred in animals exposed to RF radiation after the barbiturate injection, but not in controls. Similar but more pronounced effects were seen at 2 mW/cm^2 (SAR estimated at 0.2 W/kg). In this study, the EEG was recorded with the aid of implanted stainless steel electrodes.

Recently, Thomas et al. (1979) reported that acute, low level (av 1 mW/cm^2) 2450-MHz (PW) radiation in the near field (SAR estimated at 0.2 W/kg) potentiates the behavioral response to chlordiazepoxide (a tranquilizer) in rats. This was primarily a behavioral study and is discussed in § 5.5, Behavior.

It can be concluded from such pharmacologic studies that low level microwaves may interact in a specific manner on the nervous system in conjunction with drugs. Such interactions may prove potentially to be both useful and harmful as more information becomes available.

5.4.4 Effects on Neurotransmitters

Specific neural systems that contain various neurotransmitters are known to affect the inhibitory or excitatory states of the brain. The relative firing rates of these neuronal systems is reflected in the turnover of their neurotransmitters. Since RF radiation has been reported to stimulate and depress the CNS, several scientists have investigated the effects of RF radiation on CNS neurotransmitters.

Snyder (1971) made neurochemical measurements in rats exposed to 3000-MHz (CW) radiation. He observed that a 1-h exposure at 40 mW/cm^2 (SAR estimated at 8 W/kg) resulted in a significant increase of 5-hydroxyindolacetic acid (5-HIAA) and 5-HT (serotonin) in discrete nuclei of the brain. The opposite effect, that is, reduced levels of 5-HIAA and 5-HT, was found in rats exposed at 10 mW/cm^2 (SAR estimated at 2 W/kg) 8 h/day for 7 days. The body temperature in the rats exposed at 10 mW/cm^2 rose by 1 to 2 °C during irradiation, and the animals showed signs of moderate heat stress. To compare the effects of microwave exposure (10 mW/cm^2) to those of conventional radiant heat loads, rats were placed in an incubator maintained at 34 °C by thermostatically controlled incandescent lights for 8 h/day for 7 days. Body temperature was raised to the equivalent of that observed after irradiation at 10 mW/cm^2. No difference was found in the turnover rate of norepinephrine or 5-HT or steady state levels of 5-HIAA between heated and control animals. Snyder concluded that exposure to RF-radiation produced distinctly different effects on 5-HT and 5-HIAA in rat brains than conventional heating.

Zeman et al. (1973) investigated the effects of acute and chronic exposure of rats to 2860-MHz (PW, average power 300 W) radiation on rat brain gamma-aminobutyric acid (GABA). Chronic exposures were conducted for 4 to 6 weeks, 4 to 8 h/day, at 10 mW/cm^2 (SAR estimated at 2 W/kg). Acute exposures were conducted at 40 to 80 mW/cm^2 power density (SAR estimated at 8 to 16 W/kg) for 5 or 20 min. No significant change in body temperature was noted during chronic exposures at 10 mW/cm^2, while rectal temperature increased by 3 °C after acute exposures at 40 to 80 mW/cm^2. There was no significant difference in whole-brain GABA levels between control and irradiated animals in acute or chronic experiments. These results would be more meaningful if the investigation had focused on discrete areas of the brain rich in GABA, rather than whole brains; however, others have used the procedure of whole-brain assays successfully.

Merritt et al. (1976) reported a decrease in norepinephrine, dopamine, and serotonin in discrete areas of rat brains after whole-body exposure for

10 min to 1.6-GHz microwaves at 80 mW/cm^2 (SAR estimated at 24 W/kg). These exposures raised rectal temperatures by 3.7 °C. Hypothalamic epinephrine decreased significantly in irradiated and hyperthermic controls, although serotonin levels decreased in hippocampi of irradiated rats but not in those of control hyperthermic rats. There were no differences in the serotonin contents in the hypothalamus and striatum between hyperthermic controls and irradiated animals. Merritt _et al_. concluded that hyperthermia was responsible for the effects on neurotransmitters.

In a separate study, Merritt _et al_. (1977) observed a decrease in rat hypothalamic norepinephrine and dopamine after a 10-min exposure to 1.6-GHz microwaves at 20 mW/cm^2 (SAR estimated at 6.0 W/kg), but not at 10 mW/cm^2. The higher power density was associated with increased temperature, whereas the lower was not. Serotonin in the hypothalamus was unaffected by microwaves even at power densities as high as 80 mW/cm^2. No comment was made on hippocampal levels of serotonin in this study.

The effect of RF radiation on calcium ion efflux from brain and other tissues is discussed in § 5.7.5, Calcium Ion Efflux.

5.4.5 Unresolved Questions

The effects of low-level exposure to RF radiation on the development of the CNS need much greater attention. Thus far, only gross brain teratologic and brain-weight studies have appeared in the literature. Investigations on subtle effects of RF radiation on CNS development are lacking. The effects on the growth and maturation of the nervous system at the cellular and subcellular levels need to be examined. Albert et al. (1981) reported permanent loss of cerebellar Purkinje cells in rat pups after exposure of pregnant dams to 100-MHz (CW, SAR = 2.77 W/kg) and 2450-MHz (CW, SAR = 2 W/kg) radiation. These authors reported a reversible decrease in cerebellar Purkinje cells if newborn rat pups were exposed to 2450-MHz radiation.

Synergistic and antagonistic effects of RF radiation with alcohol, x-rays, and other agents should be investigated, since some findings already indicate that this area should not be ignored.

Nervous system effects are summarized in Table 5-12. There appear to be ample data that suggest effects of RF radiation on the nervous system of animals and humans. On the other hand, data on the BBB are controversial. Long-term low level studies on the adult nervous system are conspicuously lacking in the U.S. In addition, information on the effects of chronic, low level RF-radiation exposure on neurotransmitters is lacking.

In summary, the state of the art does not permit one to assume that exposure to low level RF radiation produces a significant effect on nervous system morphology, the blood-brain barrier, CNS-active drugs, or neurotransmitters. Since chronic low level studies are lacking in this country, great care must be taken when making judgments until long-term studies are completed.

TABLE 5-12. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON THE NERVOUS SYSTEM*

		Exposure Conditions				
Effects	Species	Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	Reference
Desynchronized EEG	Rabbit	3000 (PW)	20 (av)	1 x 20	3.0 (est)	Edelwejn (1968)
Lowered tolerance to CNS stimulating drug	Rabbit	3000 (PW)	7 (av)	24-26 x 180	1.0 (est)	Edelwejn (1968)
Biphasic effect on the potency of a convulsive drug	Mice	3000 (PW)	5	8-36 x Unknown	-	Servantie _et_ _al_. (1973)
Changes in EEG patterns of anesthetized animals	Rabbits	9300 (CW)	0.7-2.8	1 x 5	0.1-0.3 (est)	Goldstein and Sisko (1974)
Potentiation of drug response	Rats	2450 (PW)	1.0 (av)	1 x 30	0.2 (est)	Thomas _et_ _al_. (1979)
Decreased brain NE, DA, serotonin in hyperthermic animals	Rats	1600 (CW)	80	1 x 10	24 (est)	Merritt _et_ _al_. (1976)
Decreased hypothalamic NE, DA, serotonin	Rats	1600 (CW)	20, 80	1 x 10	6-24 (est)	Merritt _et_ _al_. (1977)
No effect on neurotransmitter levels	Rats	1600 (CW)	10	1 x 10	3.0 (est)	Merritt _et_ _al_. (1977)
No effect on GABA content	Rats	2860 (CW)	80 40 10	1 x 50 1 x 20 24-56 x 240-480	16.0 (est) 8.0 (est) 2.0 (est)	Zeman _et_ _al_. (1973)

(continued)

TABLE 5-12. (continued)

Effects	Species	Exposure Conditions Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	Reference
Swollen neurons in specific brain regions	Chinese hamsters	2450 (CW)	25-50 25	1 x 30-1440 22 x 840	3.5-17.5 (est) 8.8	Albert and DeSantis (1975)
Swollen neurons in hypothalamus and subthalamus	Chinese hamsters	1700 (CW)	10, 25	1 x 30-120	5, 12.5 (est)	Albert and DeSantis (1976)
Myelin figures in dendrites 6 weeks post-exposure	Rats	2450 (CW)	23	110 x 300	2.3	Switzer and Mitchell (1977)
Increased permeability of BBB to fluorescein	Rats	1200 (CW) 1200 (PW)	2.4 0.2 (av)	1 x 30 1 x 30	1.0 (est) 0.08 (est)	Frey *et al*. (1975)
Myelin degeneration and metabolic alterations in glial cells	Guinea pigs	3000 (CW)	3.5-25	-	0.5-3.5 (est)	Baranski (1972b)
	Rabbits	3000 (CW)	5		0.4-2.8 (est)	
Focal areas of increased BBB permeability to peroxidase	Chinese hamsters	2450 (CW)	10	1 x 120-480	2.0	Albert (1979b)
	Rats	2450 (CW)	10	1 x 120-480	0.9	
Brain temperature elevation (40-45 °C); increased permeability of BBB	Rats	2450 (CW)	80 W	1 x 10-30	-	Sutton and Carroll (1979)
Increased permeability of BBB (mannitol and inulin)	Rats	1300 (CW) 1300 (PW)	1.0 0.3 (av)	1 x 20 1 x 20	0.4 0.1	Oscar and Hawkins (1977)

(continued)

TABLE 5-12. (continued)

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
EEG effects seen after chronic but not acute exposures	Rabbit	1-10 (AM)	60-500 V_{rms}/m	1 x 120-180	10^{-5}-10^{-4}	Takashima *et al*. (1979)
		1-10 (AM)	90-500 V_{rms}/m	20-30 x 120-180	10^{-4}-10^{-3}	
EEG changes	Cat	147 MHz (AM)	0.8	-	-	Bawin *et al*. (1973)
Reversible neuronal morphology alterations	Rat	3 GHz	10	-	1.6 (est)	Gordon (1970)
	Rat	3 GHz	10	-	1.6 (est)	Tolgskaya and Gordon (1973)
No major changes in CNS; only mild pyknosis of some neurons (brain temperature ~ 43 °C)	Rat	2.45 GHz	-	-	-	Austin and Horvath (1954)
Changes in brain neurotransmitters	Rat	3 GHz	40 10	1 x 60 7 x 480	8.0 (est) 2.0 (est)	Snyder (1971)

*AM = amplitude modulation, NE = norepinephrine, DA = dopamine.

5.5 BEHAVIOR

Michael I. Gage

5.5.1 Introduction

Behavior has been defined as "anything an organism does" (Catania 1968), or as "the actions or reactions of persons or things under specified circumstances" (Morris 1976). Behavior may also be defined as the actions of an organism in relation to its environmental stimuli.

Behavioral effects of RF radiation have been extensively studied for several reasons. The first is the reports of experiments (not fully documented with methods and detailed data analysis) from the Soviet Union and other European countries that behavioral effects of microwaves are seen at relatively low levels, i.e., 500 $\mu W/cm^2$ and below at 2375 MHz in rats (Dumansky and Shandala 1974; Shandala *et al*. 1977). The second is that behavior can serve as an index of total organism functioning, especially by elucidating the integrative status of the nervous system as well as that of other organ systems of the body. Moreover, behavior can be analyzed in a nonterminal fashion, without resort to surgically or biochemically invasive preparatory techniques.

Behavior may be separated into two major categories: naturalistic and acquired. Spontaneous or naturally occurring behavior may be innate and is often species-specific in frequency of occurrence. Examples of naturally occurring behavior include locomotor activity, eating, drinking, and mating.

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There are two general categories of acquired or learned behavior--respondent and operant, which are distinguished by the procedures used in the acquisition or conditioning of the behavior. Respondent conditioning occurs as a consequence of the temporal contiguity between stimuli. Stimuli paired in time with another stimulus, which reflexively elicits a response, gradually elicit the response. Examples of acquired respondent behavior are salivation and hunger pangs when passing a restaurant or eye blinks to acoustic stimuli. Responses conditioned by respondent procedures are usually measured by their occurrence and their magnitude.

Much complex behavior of human beings and other higher animals in the course of daily activities can be viewed as emitted or operant behavior. Operant conditioning occurs as a consequence of reinforcement that follows the emission of a response. Reinforcers may be positive (such as food or water), or negative (such as termination of electric shock or intense radiant energy). All reinforcers maintain or increase the frequency of response. By definition, a positive reinforcer is a stimulus that increases or maintains the probability of emission of an operant by its presentation. A negative reinforcer is a stimulus that increases or maintains this probability by its removal after emission of the operant. Reinforcement need not follow the occurrence of each response. It may be intermittent according to a schedule (i.e., a schedule of reinforcement). Responses are said to be conditioned when they have a highly predictable probability of occurrence. This probability is often expressed by the average occurrence within a period of time, or the response rate. Examples of operant behavior include eating with a knife and fork, driving a car, or writing a review on behavioral effects of microwaves.

Operant conditioning may be used to answer specific questions about behavior that may be similar across species. For example, by reinforcing the responses in the presence of light of one wavelength but not reinforcing responses in the presence of light of any other wavelength, animals can learn to respond selectively in the presence of light of the first wavelength. By presenting light at wavelengths close to the one that is reinforced, the threshold for discriminability of colors can be obtained.

Specific types of behaviors investigated in behavioral research are so numerous that no attempt can be made to describe all of them here. Descriptions will be given of behaviors that have been studied as a function of microwave exposures. For a more complete description of behavior as studied by ethologists and psychologists, the reader is referred to several standard books (Brown 1975; Hinde 1970; Honig and Staddon 1977; Kling and Riggs 1971; Konorski 1967; and Pavlov 1960).

5.5.2 Summary

Some general statements can be made regarding the effects of RF-radiation exposure on behavior:

- Some microwave effects have been reported on various kinds of animal behavior. Although most of the studies have used rats as subjects, a few have used mice, squirrel monkeys, and rhesus monkeys.

- Changes in locomotor behavior have occurred after CW exposures at an SAR as low as 1.2 W/kg in rats (D'Andrea et al. 1979). Changes in food and water intake or body mass have not been consistently reported at such levels.

- Decreases in rates of ongoing operant behavior have been seen during exposures at SAR = 2.5 W/kg in rats (de Lorge and Ezell 1980), and cessation of operant behavior has been seen at an SAR of 10 W/kg in rats (D'Andrea et al. 1976).

- Alterations in operant performance measured after exposure was terminated also occurred with SAR's of 2.5 W/kg or more in rats (Gage 1979a).

- The threshold for detection of microwaves may be as low as 0.6 W/kg in rats (King et al. 1971). However, it is not certain that animals avoid or attempt to escape from CW microwaves except at very high power levels.

- Drug effects on behavior in rats have been augmented after PW-radiation exposures lasting 0.5 h at average SAR = 0.2 W/kg (Thomas et al. 1979). Behavioral thermoregulation has been altered after only several minutes of exposure at SAR = 1.0 W/kg in the rat (Stern et al. 1979) and at SAR = 1.0 W/kg in the squirrel monkey (Adair and Adams 1980b).

- Although the same behavioral effects during or after microwave exposure of the same magnitude may not be consistently predictable, enough behavioral changes have been reported after similar exposures to warrant the conclusion that behavior is disrupted by microwaves with an energy input that approximates one quarter to one half of the resting metabolic rate of many animals.

- These behavioral alterations are reversible with time.

5.5.3 Naturalistic Behavior

Spontaneous locomotor behavior has been studied with both acute- and chronic-exposure regimens in the rat. Hunt et al. (1975) found decreased initial exploratory activity by male Wistar rats after a 30-min exposure to 2450-MHz fields in a multimodal cavity with power adjusted to produce an SAR of 6.3 W/kg. The activity of exposed animals returned to control values within a 2-h period. The decrease in initial exploratory activity was the same whether the rat was placed in the apparatus immediately after or 1 h after exposure was terminated. Core body temperature was increased to 40.3 °C at termination of exposure but dropped to 37.8 °C, within the normal range, 1 h after exposure. Decreased swimming speed in water at 24 °C was also seen in rats that were practiced swimmers after 30-min exposures to 2450-MHz fields at SAR's of either 6.3 or 11 W/kg. The effects were seen only after 1.2 km of swimming following a 6.3-W/kg exposure; after an 11-W/kg exposure, effects were seen immediately for the first few meters and again after 0.6 km of swimming despite the fact that water at 24 °C would reduce persistence of a microwave-related hyperthermia.

Roberti _et_ _al_. (1975), on the other hand, did not see changes in spontaneous motor activity, as measured in a glass cage, in male Wistar rats after four different exposure conditions in the far field of an anechoic chamber. The locomotor activity measured by Roberti _et_ _al_. may not have required as much physical effort as continuous swimming. Exposures (estimates of SAR values based on single animal exposures) were either to 10,700-MHz (CW) fields at 0.6 to 0.9 mW/cm^2 (SAR estimated at 0.15 W/kg) for 185 continuous hours (24 h daily for 7 2/3 days); to 3000-MHz (CW) fields at 0.5 to 1.0 mW/cm^2 (SAR can be estimated at 0.3 W/kg) for 185 continuous hours; to 3000-MHz (PW) fields, 769 pulses/s, at 1.5 to 2.0 mW/cm^2 (SAR estimated at 0.6 W/kg) for 185 continuous hours; or to 3000-MHz (PW) fields, 769 pulses/s at 24 to 26 mW/cm^2 (SAR estimated at 8.3 W/kg) for 408 continuous hours (24 h daily for 17 days). After this last exposure condition, no change was also observed in running speed during forced runway running by the rats.

Locomotor activity on a small platform was increased (as compared with five controls) in five female Sprague-Dawley rats during the course of repeated exposures to 2450-MHz (CW) fields in a multimodal cavity (Mitchell et al. 1977). Exposures of 5-h duration occurred 5 days weekly for 22 weeks. The average SAR was determined to be 2.3 W/kg, which is similar to the SAR at power density of 10 mW/cm^2 in a plane-wave environment. The activity increased within the first week of exposure and remained high throughout the course of the exposure period.

Decreases in activity, measured by visual observation, were reported during repeated exposures of eight Wistar male rats to 918-MHz (CW) fields in a circular waveguide (Moe et al. 1976). Each exposure lasted 10 h (from 2200 to 0800) and occurred nightly for 3 weeks (total of 210 h), and the range of whole-body average SAR's was measured as 3.6 to 4.2 W/kg (10 mW/cm^2 average power density). The decreased activity predominantly occurred shortly after the microwave field was activated. The exposed rats were stretched out in a prone position more frequently than control rats in the early morning hours. In addition, exposed rats were reported to consume less food than did the controls over the course of the exposure, even though their body mass was not different from that of controls. A repeat of this experiment where eight male Wistar rats received an average SAR of 0.9 to 1.0 W/kg (average power density of 2.5 mW/cm^2; daily 10-h exposures lasting for 13 weeks) resulted in no differences in food consumption or in activity measured during the eleventh week (Lovely et al. 1977). The two studies indicate that a dose-rate-related threshold for these effects might be somewhere between 1.0 and 3.6 W/kg. Unfortunately, in the circular waveguide, the power density is twice the average on axis and falls off rapidly toward the wall, resulting in the possibility of fluctuating and uncertain quantitative description of SAR at specific times during exposure (Guy and Chou 1976).

Effects on spontaneous behavior of rats were reported in two other chronic exposure experiments. Both experiments used 15 exposed and 15 control male Long-Evans rats irradiated from 0900 to 1700 (8-h), 5 days weekly for 16 weeks in an anechoic chamber with a central monopole antenna and ground plane. The rats were adapted to the exposure and testing apparatus for 4 or 8 weeks before irradiation. In one experiment, exposures were to 2450-MHz (CW) fields at an average SAR of 1.2 W/kg (power density, 5 mW/cm^2) (D'Andrea _et_ _al_. 1979); and in the other, exposures were to 915-MHz (CW) fields at an average SAR of 2.5 W/kg (power density, 5 mW/cm^2) (D'Andrea _et_ _al_. 1980).

In the study at 2450 MHz, rats showed decreases in activity as measured on a stabilimetric platform throughout the course of exposure but increased running-wheel activity overnight through the course of exposure (this latter effect was not significant). No significant differences were seen in food and water intake and in body mass. In the study at 915 MHz, exposed rats showed increased activity as measured both in the running wheels and on the stabilimeter. Again, no significant changes in food and water intake or body mass were observed.

Rudnev _et_ _al_. (1978) reported effects of exposure of 25 male albino rats to 2375-MHz (CW) fields at 0.5 mW/cm^2 (SAR estimated at 0.1 W/kg for individual animal exposure) for 7 h daily for 1 month. Open field activity was measured in irradiated rats and in 25 controls as the number of squares crossed in 3 min on 2 successive days. The count on the first day was defined as exploratory activity, whereas that on the following day was defined as motor activity. Shock-induced aggression was measured by observing battles between an exposed and control rat. Maintenance of balance on a rotating treadmill (dynamic-load endurance) and on an inclined rod (static-load endurance) was measured, as was the amount of food consumed in 20 min after 23 h of deprivation. Electrodermal skin sensitivity was measured as the voltage of 100-Hz square-wave electrical stimulus that was needed to elicit paw withdrawal from the metal bars on the cage floor. Measurements were made prior to irradiation on the 10th, 20th, and 30th days of exposure, and every 15 days for 3 months after exposure.

A significant reduction in food intake, time on the treadmill, and in time on the inclined rod was seen by the 10th day of exposure. Exploratory activity was significantly decreased, and shock sensitivity was increased after 20 days of exposure. At the end of exposure, exploratory and motor activity, time on the inclined bar, and shock sensitivity were significantly decreased. The latency to start eating was increased for 30 days after exposure ended. Time on the treadmill was reduced for 15 days after the termination exposure. Exploratory activity was increased throughout a 3-month postexposure period. Sensitivity to electric shock was reduced significantly on the 30th and 60th day after exposure ended and was still below control levels on the 90th day.

5.5.4 Learned Behavior

5.5.4.1 Respondent Conditioning--

Currently, there appear to be no reports by U.S. investigators of microwave exposure altering respondent behavior, although an experiment using microwaves as an unconditional stimulus has been published. Some studies using respondent conditioning techniques that report changes in behavior as a consequence of microwave exposure appear in the Soviet literature (e.g., Dumansky and Shandala 1974; Lobanova 1974). Unfortunately, details regarding exposure conditions or behavioral methodology and results are too sketchy to permit inclusion in this review. An attempt was made to use microwave exposure as an unconditional stimulus in one experiment (Bermant et al. 1979). A 30-s presentation of a 525-Hz tone that preceded 2450-MHz sinusoidally modulated microwaves that were either presented for 10 s (SAR = 420 W/kg) or 30 s (SAR = 220 W/kg) or that preceded an electric shock to the tail produced rises in rectal temperature of 0.7 C, 0.5 C, or 0.37 °C, respectively, during a base-line period over the course of 10 conditioning sessions. Control female Sprague-Dawley rats presented with the tone alone showed a decrease of 0.47 °C in rectal temperature during this period. The microwave exposure itself was designed to produce an increase in rectal temperature of 1.5 °C. Aside from this study there are no reports of microwaves altering respondently conditioned behavior in which exposure parameters allow clear determinations of the SAR.

5.5.4.2 Operant Conditioning--

There is a large body of literature examining alterations of operant behavior produced by microwaves for which SAR values have been, or can be, determined.

Reduction in rates of responding on an operantly conditioned task has been observed during the course of microwave irradiation. Rats were trained to lever-press for food pellets on a random-interval, 30-s schedule. After behavior on this task stabilized, the rats showed a response rate that was in general linearly uniform and typical of random- or variable-interval schedule-controlled performance. The rats were then exposed to microwaves under each of several conditions in sessions lasting 25 min, or until the rat's response rate fell below one third of its base-line control rate. In an initial experiment (D'Andrea et al. 1976), six male Long-Evans rats were exposed to 360-, 480-, or 500-MHz (CW) fields in a parallel-plate apparatus at an incident power density of 25 mW/cm^2 (the long axis of the rat was parallel either to the electric-field vector or to the vector of wave propagation). Responding was reduced only during exposures to 500-MHz fields when the long axis of the body was parallel to the electric-field vector. Behavior stopped abruptly after ~ 11 min of exposure, and upon removal from the apparatus the animals appeared flaccid, wet, and, according to the authors, heat stressed. At this exposure the SAR was computed from the measured 0.16 °C/min rise in rectal temperature to be ~ 10 W/kg. Exposures that produced no change in behavior had SAR's ranging from 5 to 6 W/kg.

In a second experiment (D'Andrea et al. 1977), these results were confirmed and extended. Exposures were conducted in a monopole-above-ground radiation chamber and lasted for up to 55 min, or until responding on the random-interval schedule fell below one third of the base-line rate. Exposures of five male Long-Evans rats for periods up to 55 min to 400-, 500-, 600-, and 700-MHz (CW) fields at 20 mW/cm^2 power density and 22 ± 1 °C ambient temperature yielded a U-shaped function of time to the criterion of reduction in rate, with the minimum of ~ 23 min at 600 MHz when rectal temperature increased 0.09 °C/min (SAR estimated at 16.4 W/kg). At the time they stopped responding all rats appeared heat stressed and were engaged in spreading saliva on their fur. Six additional rats, exposed at 600-MHz (CW) fields at power densities of 5, 7.5, 10, and 20 mW/cm^2, showed decreased times to stop their responding, at power densities above 7.5 mW/cm^2 when rectal temperature increased 0.04 °C/min or more. At 10 mW/cm^2 (SAR estimated at 7.5 W/kg) the rats stopped responding after ~ 45 min, and rectal temperature increased 0.04 °C/min. Three rats exposed to PW microwaves with 170 mW/cm^2 peak and 5.10 mW/cm^2 average power density showed no change in performance. As in the earlier experiment of D'Andrea _et_ _al_. (1976), response reduction was abrupt and was correlated with the rectal temperature increase.

A series of experiments by de Lorge (1976, 1979) also examined alterations in operant performance during exposure to microwaves. In most of these experiments, the schedule of reinforcement was used to measure observing and detection responses in a vigilance task. Two levers were present in a testing chamber or in front of a primate restraint chair made of Styrofoam and sheet plastic for optimal transparency to microwaves. Responses on the right lever, called observing responses, produced either a low- or a high-frequency acoustic signal. The high-frequency signal was scheduled to occur on a variable interval of either 30 or 60 s. If the animal made a response on the left lever when the high-frequency signal occurred--a detection response--it received a food pellet as a reinforcer. Observing responses occurred at fairly linear response rates, a pattern similar to that seen on variable interval schedules of reinforcement.

In the first experiment (de Lorge 1976) five male rhesus monkeys (Macaca mulatta) showed no change in behavior on this schedule during 1 or 2 h of exposure to 2450 MHz in the far field of an anechoic chamber when power densities ranged to 16 mW/cm^2 (SAR estimated at 1.2 W/kg). The field was 100 percent amplitude modulated at 120 Hz. Three of these monkeys showed reduced rates of observing response during 1-h exposure to this field at 72 mW/cm^2 (SAR estimated at 5.0 W/kg) but not at 32, 42, 52, or (in two monkeys) 62 mW/cm^2. At 72 mW/cm^2, rectal temperatures rose ~ 2 °C, and were still increasing at the end of the hour-long session. The animals moved more in their chairs after 20 min, and were observed to take short naps after ~ 30 min at this power density. When observing responses decreased, reaction time to respond on the left lever increased.

In the second experiment (de Lorge 1979) four male squirrel monkeys (Saimeri sciureus) were tested and exposed to 2450-MHz 120-Hz modulated microwaves under conditions similar to those described above at 10, 20, 30, 40, 50, 60, and 70 mW/cm^2. No reduction in the mean rate of right-lever observing responses > 1 standard deviation below the mean of the control rate was seen at any power density during the 30-min exposures. But brief pauses in responding were seen at microwave onset and offset at 50 mW/cm^2 and above

(SAR estimated at 2.75 W/kg). At this power density rectal temperature rose > 1 °C. Three of the monkeys were also given 1-h exposures. Observing response rate seemed to decrease more, and, according to an impression gained from performance of one monkey (de Lorge 1979, Figure 6), this decrease began earlier in sessions at higher power densities. One of the three monkeys exhibited an increase of response rate as power densities increased. After microwave exposure, all monkeys also showed decreased responding that was directly related to the power density. All monkeys showed increase in frequency of incorrect responding on the left lever for food, which was a direct function of power density. Reliable changes in behavior were considered to occur only at power densities of 40 to 50 mW/cm^2 at a time when rectal temperatures had risen by > 1 °C.

In a third experiment (de Lorge and Ezell 1980) eight male Long-Evans rats were exposed to 5620-MHz (PW) fields at 662 pulses/s, and then to 1280-MHz (PW) fields at 370 pulses/s. They were tested on the behavioral task of vigilance during exposures (SAR's were reported at 0.19 W/kg per mW/cm^2 at 5620 MHz, and 0.25 W/kg per mW/cm^2 at 1280 MHz). Rates of observing responses during exposures to 1280-MHz fields decreased somewhat at 10 mW/cm^2 (average power density), and decreased markedly after 15 to 20 min during 15 mW/cm^2. At 5620 MHz, rates of observing responses decreased only during exposures at 26 mW/cm^2 and above. Behavior decrements occurred at SAR = 2.5 W/kg at 1280 MHz but required SAR = 4.9 W/kg at 5620 MHz.

In a related experiment (Sanza and deLorge 1977), four male Sprague-Dawley rats were trained to respond on a fixed-interval 50-s schedule for food pellets as reinforcers. With this schedule, the first response emitted 50 or more seconds after arrival of the last food pellet produced another food pellet. Exposures for 60 min to 2450-MHz, 120-Hz modulated at fields at 37.5 mW/cm^2 in the far field of an anechoic chamber produced decreases in response rates that had a fairly abrupt onset. The response decrements were seen only in two rats that had high base-line rates and not in two rats with low response rates. Exposures at 8.8 and 18.4 mW/cm^2 produced no decrements in performance. All rats spent more time at the wall opposite the food cup during 18.4- and 37.5-mW/cm^2 exposures than during sham or 8.8-mW/cm^2 exposures. The SAR was not given but is estimated at 3.7 W/kg at 18.4 mW/cm^2 and 7.5 W/kg at 37.5 mW/cm^2.

Responding of three male rhesus monkeys trained to a high level of proficiency on a visual tracking task was not disrupted by exposures at 10 or 20 mW/cm^2 to 1200-MHz (CW) fields (reported SAR estimated at 0.8 and 1.6 W/kg) during behavior sessions lasting ~ 2 h (Scholl and Allen 1979).

Some other studies have looked at changes in previously learned operant behavior at the termination of single or multiple exposure periods. Thomas et al. (1975) trained four male Sprague-Dawley rats to respond on a multiple schedule. One component was fixed ratio 20 (FR20): every 20th response on the right lever was reinforced by a food pellet. The other component was a differential-reinforcement-of-low-rate of 18 s with a limited hold of 6 s (DRL 18 LH 6): Responses on the left lever separated by at least 18 s, but by no more than 24 s, were reinforced. Components alternated on an irregular basis. Only one of the schedules was in effect during a given time period.

Exposures to microwaves lasted for 30 min, and behavioral testing began 5 to 10 min after exposure. Exposure parameters were as follows: 5, 7, 15, and 20 mW/cm^2 at 2450-MHz (CW) fields; 5, 10, 15, and 20 mW/cm^2 at 2860-MHz (PW) fields at 500 pulses/s and 1-μs pulse width; and 1, 5, 10, and 15 mW/cm^2 at 9600-MHz (PW) fields at 500 pulses/s and 1-μs pulse width. All rats were exposed to all parameters while restrained in the far field of an anechoic chamber. In general, response rates increased on the DRL schedule and decreased on the FR schedule. Increased rates on the DRL schedule were seen following exposures to 5 mW/cm^2 and above at 9600-MHz fields (SAR estimated at 1.5 W/kg), 7.5 mW/cm^2 at 2450-MHz (CW) fields (SAR estimated at 2.0 W/kg), and 10 mW/cm^2 and above at 2860-MHz fields (SAR estimated at 2.7 W/kg). Decreased response rates on the FR schedule were measured following exposures to 5 mW/cm^2 and above at all frequencies (SAR estimated at 1.5 W/kg for 9600 MHz, and 1.4 W/kg for 2450 and 2860 MHz). Increased response rates during time-out periods between components were seen following 5 mW/cm^2 at all three frequencies. Time-out responses peaked and then dropped after exposures at higher power densities.

In a second study, Thomas _et al_. (1976) trained four male Sprague-Dawley food-deprived rats on a fixed-consecutive-number-eight (FCN 8) schedule. With this schedule, at least eight presses had to be made on the right lever before depression of the left lever would yield a food pellet reinforcer. If the rat made fewer than eight consecutive responses on the right lever before switching, the count was restarted at zero. Well trained rats were tested after 30-min exposures in the near field at 5, 10, and 15 mW/cm^2 to 2450-MHz (PW) fields at 500 pulses/s, and 1-μs pulse width. Because exposures were in the near field, SAR cannot be precisely estimated but may be assumed at 0.4 W/kg for each mW/cm^2 (Durney _et_ _al_. 1980). The percentage of eight or more consecutive responses on the right lever (reinforced runs) decreased, and the length of these runs decreased after all exposures. Those decreases were direct functions of power density. However, the overall rate of responding and the running rate (i.e., the rate after the first response following reinforcement) hardly decreased during these postexposure sessions.

Gage (1979a) reported decreases in response rates of eight adult male Sprague-Dawley rats trained to alternate between levers either 11 or 33 times for a food-pellet reinforcer. The decrements occurred in sessions following overnight, 15-h exposures to 2450-MHz (CW) fields at 10, 15, and 20 mW/cm^2, but not after exposures at 0.5 and 1.0 mW/cm^2. Only very small decrements were seen after 55-min exposures at power densities to 30 mW/cm^2 (the SAR measured in rats under similar exposure conditions was 0.3 W/kg per mW/cm^2).

Vigilance discrimination was tested immediately after 30 min of irradiation in 10 well trained, young adult male Wistar rats (Hunt _et_ _al_. 1975). Exposures produced SAR's of 0.0, 6.5, and 11.0 W/kg at 2450 MHz (modulated in a quasi-sinusoidal fashion at 120 Hz in a multimodal cavity). All rats were exposed at both SAR values, but the sequence of exposures was varied. The task required the rats to obtain saccharin-flavored water reinforcers by pressing a bar when a light flashed, but by not pressing a bar when a sonic stimulus was presented. One of the two stimuli was presented every 5 s, and the light was presented 12.5 percent of the time. Rats at both SAR's had an increased number of omission errors (i.e., failures to respond to the light after exposure), but there were no increases in errors of comission (i.e., responding wrongly when the noise was presented). The failure to correctly respond was more frequent at the start of the session, as well as after exposure at the higher SAR.

Schrot *et al*. (1980) experimented with three male albino rats trained to learn a new sequence of pressing three levers for food reinforcers daily in repeated-acquisition procedure. The rats increased their number of errors and decreased their rate of sequence completions when tested immediately after 30-min exposures to 2800-MHz (PW) fields (500 pulses/s, 2-μs pulse width) at 5 and 10 mW/cm^2 average power density. No effects were seen at lower average power densities of 0.25, 0.5, and 1 mW/cm^2. Peak powers were 0.25, 0.5, 1, 5, and 10 W/cm^2 in these exposures. The rats were exposed in a sleeve holder with the electric-field vector perpendicular to the long axis of the animal's body. The reported SAR's based on temperature measurements were 0.7 and 1.7 W/kg at 5 and 10 mW/cm^2, respectively.

Operant behavior has also been examined during or following the course of chronic microwave exposures in some reports also described in §5.5.3, Naturalistic Behavior. Mitchell *et al*. (1977) measured performance on two schedules in separate groups of rats pretrained before the start of 22 weeks of 5-h exposures, 5 days/week, to 2450-MHz fields (average SAR at 2.3 W/kg) in a multimodal cavity. Five exposed and five control female Sprague-Dawley rats were tested for 30-min sessions on a schedule of multiple FR5 extinction for 15 s (MULT FR5 EXT 15 s). When a white lamp was on, every fifth response was reinforced by a food pellet, but during periods when the lamp was off, no responses were reinforced. Although the control rats had higher response rates during the FR component, this difference was not significant. Exposed rats had higher response rates than controls during the extinction component, and this difference was statistically significant. The ratio of response rate during the MULT-FR5 component to response rate during the EXT-15-s component was significantly different in exposed as compared with control rats: Exposed rats exhibited a higher ratio, indicating poorer discrimination over the course of exposure, although they had a value like that of the control rats before irradiations began. Another schedule, Sidman avoidance, was used to test escape and avoidance response. Five exposed and four control rats were trained to postpone an unsignaled 2.0-mA foot shock for 15 s (response-shock interval) by pressing a lever. During 30-min sessions, the animals received a shock every 0.5 s (shock-shock interval) until they pressed the lever. No significant effects of microwave exposures were seen with this schedule, although improvement in avoidance was seen in all rats both within and over the course of testing sessions.

Conditioned taste aversion was studied in experiments reporting chronic exposures of rats to 918-MHz fields in circular waveguides at 10 mW/cm^2 (Moe _et_ _al_. 1976) and 2.5 mW/cm^2 (Lovely _et_ _al_. 1977). Rats were given a saccharin solution to drink in place of water during the microwave exposure period. Presumably, if the saccharin were drunk in conjunction with an agent, such as microwave radiation, which made the rat sick or produced some undesirable sensations, this connection would be learned and the solution would be avoided in the future. Preference was measured after exposure by allowing a water-deprived rat to choose between drinking the saccharin solution and water for 20 min. In the experiment at 2.5 mW/cm^2 (Lovely _et_ _al_. 1977), saccharin preference was tested only from the 9th to the 13th week of exposure. No difference between exposed and control rats was seen in amount of saccharin solution consumed either at 2.5 mW/cm^2 (average measured SAR at 1.0 W/kg) or at 10 mW/cm^2 (average measured SAR at 3.9 W/kg).

Several studies have investigated the ability of animals to detect or to take behavioral action to minimize, avoid, or escape from microwaves. In an early paper, King et al. (1971) showed that three irradiated and three control male albino rats could respond to 2450-MHz microwaves doubly modulated at 60 and 12 Hz as the conditioned stimulus in a measure of conditional suppression. In this experiment, rats were reinforced with sugar water on a random interval schedule for licking at a water tube. At various times during each 2-h session either a 525-Hz tone or the microwaves were presented for 1 min, and an unavoidable 0.5-s electrical foot-shock followed. Conditioned suppression to the tone was reliably indicated by no licks being emitted during the tone. Microwave dose rates of 0.6, 1.2, 2.4, 4.8, and 6.4 W/kg were substituted for the tone in some sessions. During irradiation at SAR = 0.6 W/kg one of three rats suppressed responding, at SAR = 1.2 W/kg two rats suppressed, and at SAR = 2.4 W/kg all three suppressed reliably.

Johnson et al. (1976) trained two male Wistar-derived rats to nose poke in a restraint for food pellets on an FR5 schedule in the presence of an acoustic-pulse stimulus of 7.5 kHz, 10 pulses/s, 3-μs pulse duration for 3-min periods, which alternated with 3-min periods of no stimulation during which nose pokes were not reinforced (extinction). When microwaves at 918 MHz (10 pulses/s, 10-μs pulse durations) were presented for 30-s intervals during an extinction period, or when microwaves were substituted for the auditory stimulus during reinforced periods, response rates were observed that were similar to those seen in periods when the acoustic stimulus was present. The energy density per pulse of microwaves was 150 μJ/cm^2, and the average power density was 15 mW/cm^2. (The SAR would be near 7.5 W/kg if the rats were in the far field.)

Detection of microwaves does not imply that there are affective properties of this stimulus, i.e., that they hurt or feel good. In fact, such detection may be further evidence of the RF hearing phenomenon (Frey and Messenger 1973). Indeed, in several experiments in which PW microwaves are presented during exposure, the alteration in behavior of the exposed animal might be due to effects of acoustic stimulation by the microwave pulses. Such experiments should have as a control the presentation of pulsed auditory stimuli.

Frey _et al_. (1975) experimented with female Sprague-Dawley rats exposed to 1200-MHz (PW) fields at 1000 pulses/s (0.5-s pulse duration) at an average power density of 0.2 mW/cm^2 (SAR estimated at 0.2 W/kg) and a peak power density of 2.1 mW/cm^2. Six rats spent only 30 percent of a 30-min period of exposure in an unshielded half of a Styrofoam shuttle box during the last 2 of 4 successive daily exposures. Six other rats exposed to 1200-MHz (CW) fields at 2.4 mW/cm^2 (SAR estimated at 2.2 W/kg) spent 52 percent of the time in the unshielded half of the box on these days. Six other control rats spent 64 percent of the 30-min period in the unshielded half. Only the rats exposed to PW microwaves could be said to escape from the stimulus or exhibit a modest preference, which would decrease their exposure. A similar finding was also reported to occur in male rats during exposures to a 1200-MHz (PW) field at 100 pulses/s at 0.4 or 0.9 mW/cm^2 average power densities (SAR estimated at 0.4 and 0.81 W/kg, respectively) and at 133 or 300 mW/cm^2 peak power densities (Frey and Feld 1975). These rats spent an average of only 29 percent of their time in the unshielded half in seven 90-min sessions, and this side preference was maintained throughout all 7 days. Sham-irradiated rats spent an average of 57 percent of their time in the unshielded half of the box.

Two groups of eight male Wistar rats spent more than half of each of nine weekly hour periods in the side of a shuttlebox when occupancy of that side kept a PW microwave field turned off (Hjeresen et al. 1979). The 2880-MHz field was pulsed at 100 pulses/s (3.0-μs pulse width) with a 9.5-mW/cm^2 average and 33-mW/cm^2 peak power density (SAR calculated at 2.1 W/kg). The exposure was in the far field of an anechoic chamber. A group of eight rats that could not extinguish the field and another group that received no microwaves showed no side preferences. Preference for occupancy of the side that extinguished the field increased across each weekly session. Substitution of a 37.5-MHz (PW) acoustic stimulus for the microwaves in one session resulted in the rats' spending most of the session in the side that kept the acoustic stimulus off. A continuously occurring broadband "pink" noise in the anechoic chamber prevented appearance of side preference in two other groups. In addition to confirming that rats avoid or escape from pulsed microwaves, this experiment suggests that microwaves may be detected as an auditory stimulus.

Monahan and Ho (1976) showed that male CF1 mice irradiated for 10 or 15 min at 2450-MHz (CW) fields in a waveguide when forward-power levels were stabilized at 0.4, 0.8, 1.6, 2.4, 3.2, 4.0, or 4.8 W exhibited a decline in energy absorption rate at 2.4 W and above. This decline usually occurred within the first 5 min of exposure and stabilized toward the latter part of the period. Monahan and Ho interpret the results as a behavioral action to minimize exposure to the microwaves. However, they did not directly measure any behavior. During the first 5 min of exposure the SAR's measured in this apparatus ranged from 7.7 to 65.7 W/kg. The lowest SAR at which the mice clearly altered their rates of energy absorption was 28 W/kg. In a second study Monahan and Ho (1977) showed that the SAR associated with reduction of absorption during 20 min of irradiation decreased reliably from 43.6 W/kg when ambient temperature was 20 °C, to 0.6 W/kg, when ambient temperature was 35 °C.

Videotape observations of rats and mice exposed to 2450-MHz (CW) fields at 15 mW/cm^2 for 1 h in the far field below a radiating horn in an anechoic chamber did not reveal any preferential behavior that minimized whole-body absorption rates through parallel orientation to the magnetic- as opposed to the electric-field vector (Gage et al. 1979). These observations occurred at ambient temperatures of 22 or 28 °C while the animal was held in a cuboid or cylindrical enclosure. Usually, the animals assumed a curled, sleep-like posture in the hour before the microwaves were turned on and maintained that posture throughout most of the exposure period; an exception occurred in mice exposed at 28 °C, in which case they more often assumed positions that were oriented parallel to both field vectors. The SAR of the rats without any enclosure was 3.3 W/kg at 15 mW/cm^2, independent of their orientation. The SAR of the mice when parallel to the electric-field vector was 12.3 W/kg, and the SAR when the mice were parallel to the magnetic-field vector was 6.2 W/kg, without any enclosure. The animals changed positions more frequently when some difference in SAR existed relative to the position assumed.

In a recent article, Carroll et al. (1980) reported that 20 female Long-Evans rats did not go to a marked-off floor area in a multimodal cavity to reduce the intensity of 918-MHz microwaves (modulated at 60 Hz with 3-Hz mode stirrer modulation) from 60 W/kg to either 40, 30, 20, or 2 W/kg. The mean number of entries into the marked-off "safe" area and the percentage of time spent there during 22-min sessions were not different when the microwaves were on (for five 2-min periods) or off. SAR's > 60 W/kg were associated with lethality within 8 min of continuous exposure in tests of a separate group of rats. However, in the same apparatus 10 rats quickly learned to escape from an 800-μA electric foot shock by going to this marked-off area within a 22-min session. Shocked rats would remain in this area over 90 percent of the session time.

Sanza and de Lorge (1977) noted the fact that their rats first tried to jump out of a testing chamber and then assumed a stationary position after failing to escape during exposures to 2450 MHz at 37.5 mW/cm^2 (SAR = 7.5 W/kg).

5.5.5 Interactions With Other Environmental Stimuli

Interactions of microwaves with two types of environmental stimuli have been reported to affect behavior. One of these stimulus types is chemical, specifically, several commonly used psychoactive drugs; the other is physical, e.g., ambient temperature during exposure. Response rates of rats performing on a fixed-interval 1-min schedule of reinforcement beginning 0.5 h after 2.5- to 20-mg/kg dosages of chlordiazepoxide (Librium) (Thomas _et_ _al_. 1979) were increased over control values. These increases were further augmented if an exposure at an average power density of 1 mW/cm^2 of 2450-MHz (PW) fields (500 pulses/s, 2-μs pulse width, 100-mW/cm^2 peak power density) occurred in the half hour between the injection and behavioral testing. In a second study (Thomas and Maitland 1979), the dose-response function of rats given d-amphetamine sulfate was shifted to the left after exposure to microwaves having the same parameters and conditions of exposure as those mentioned above. A shift to the left of a dose-response function indicated an increased potency of the drug. Rats in this second study were reinforced for responses separated by more than 18 s (DRL 18 s). Drug doses producing increases and decreases in response rates were lower after microwave exposures than those after no microwave exposures. Although the rat was in the near field in these studies, the dose rate measured in a Styrofoam-insulated water model was 0.2 W/kg. Thomas and Maitland (1979) also showed that 0.5-h exposure to microwaves, at the parameters indicated above, 4 days/week when amphetamine was not administered, shifted the dose-response function of this drug to the left on the fifth day when a microwave exposure did not occur. In both of these studies, exposure to microwaves alone or after saline injection had no effect on behavior. The shift to the left of a dose-response function indicated that an exposure to microwaves, which by itself did not affect behavior, acted synergistically with chlordiazepoxide or amphetamine to increase sensitivity of the organism to the drug. Similar results have not been seen with chlorpromazine or with diazepam (Valium), an analog of chlordiazepoxide, in experiments in the same laboratory (Thomas et al. 1980).

In a related experiment, Monahan and Henton (1979) showed that chlordiazepoxide and, with less consistency, chlorpromazine and d-amphetamine altered response rates of mice trained in an operant-conditioning procedure to escape from or to avoid 2450-MHz (CW) fields at an average dose rate of 46 W/kg. While this experiment showed that drug effects can interact to alter microwave exposure effects, the design of the experiment does not allow any conclusion to be drawn about interactions between drugs and microwaves on performance.

Interactions with ambient temperature and humidity were predicted by Mumford (1969). Monahan and Ho (1977) showed that reduction in the rate of energy absorption by mice exposed in a waveguide to 2450-MHz (CW) fields occurred at a low dose rate of 0.6 W/kg when ambient temperature was 35 °C but required higher doses at lower ambient temperatures. Although the mice were not directly observed, the authors presumed the mice reoriented in the microwave field to reduce the amount of absorbed energy.

Gage (1979b) showed that overnight exposures at 5, 10, or 15 mW/cm^2 to 2450-MHz (CW) fields (SAR = 0.2 mW/g per mW/cm^2) at an ambient temperature of 28 °C reduced operant response rates of rats measured the morning after exposure was terminated. Similar exposures when ambient temperature was 22 °C did not result in reduced response rates except after exposure at the highest power density.

Two reports have indicated mammals will alter thermoregulatory behavior in the presence of as little as 5 mW/cm^2 of 2450-MHz (CW) microwaves. In one (Stern et al. 1979), six male rats were trained to press a lever to switch on an infrared (IR) heat lamp for 2 s in a chamber at an ambient temperature of 3.9 to 5.3 °C. Microwaves at power densities as low as 5 mW/cm^2 reduced the rate of responding for the heat lamp. The reduction in response rate that occurred shortly after microwave onset was a direct function of power density in the range of 5 to 20 mW/cm^2 and returned to base-line values when microwaves were switched off. The rats were exposed in the near field (SAR = 0.2 W/kg per mW/cm^2).

Adair and Adams (1980b) showed that thermoregulatory behavior of the squirrel monkey (a new world primate found in equatorial jungle areas) was significantly altered at power densities as low as 6 mW/cm^2 in the far zone of a 2450-MHz (CW) field within 10 min of onset of exposure. In this study, the monkeys were trained to select a preferred ambient air temperature by making an operant response to obtain 15 s of 55 °C air when the air was otherwise 15 °C or to obtain 15 s of 15 °C air when the air was otherwise 55 °C. Preferred air temperatures ranged between 35 and 36 °C without microwaves and decreased as a direct function of the microwave power density during exposure. (The SAR in this experiment was determined calorimetrically on saline models to be 0.2 W/kg per mW/cm^2.) As in the experiment by Stern et al. (1979) with rats, preferred temperatures returned to base-line levels when the microwave field was extinguished.

The above-mentioned studies of behavioral effects caused by microwave exposure are summarized in Table 5-13.

In conclusion, there is ample evidence to suggest that microwaves alter a variety of unlearned and learned behaviors occurring during and after exposures. In most cases the behavior change can be described as a reduction in the level of ongoing activity. However, there are some situations in which increases in activity have been seen. When measured, the magnitude of behavioral change seems to be related to the power density or SAR of the exposure. Behavioral changes usually revert to base-line levels after removal of the microwave field.

5.5.6 Unresolved Questions

Most unresolved questions regarding behavioral effects of microwaves arise because observed findings have not been verified within the same laboratory or in other laboratories. Repeating a study involves high cost and the risk of failure to confirm a finding due to small unnoticed differences, e.g., between standard procedures in two laboratories. Possibly for these reasons verification has often not been attempted. However, verification and systematic replication would allow determination of the limits of conditions within which a behavioral effect may be expected, as well as definition of the range of conditions adequate to observe a threshold of effect.

TABLE 5-13. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON BEHAVIOR

Effects	Species (Weight, g)	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR* (W/kg)	
Decreased exploratory activity and swimming speed, ΔT increase 2.5 °C	Young male rat	2450 (PW, multimodal cavity 120 Hz, AM)	?	1 x 30	6.3	Hunt *et al*. (1975)
No effect on spontaneous activity or activity and forced running	Male rat (160-180)	10700 (CW) 3000 (CW) 3000 (PW) 3000 (PW)	0.6-0.9 0.5-1.0 1.5-2.0 24-26 (av)	7.7 x 1440 7.7 x 1440 7.7 x 1440 17 x 1440	0.2 0.3 0.6 8.3	Roberti *et al*. (1975)
Increased locomotor activity	Female rat (307)	2450 (CW, multimodal cavity)	10	110 x 300	2.3	Mitchell *et al*. (1977)
Decreased spontaneous activity and food intake	Male rat (360-410)	918 (CW)	10	21 x 600	3.6	Moe *et al*. (1976)
No effect on spontaneous activity or food intake	Male rat (316-388)	918 (CW)	2.5	91 x 600	1.0	Lovely *et al*. (1977)
Decreased activity on stabilimetric platform, no significant increase in wheel running	Male rat (350-375)	2450 (CW)	5	80 x 480	1.2	D'Andrea *et al*. (1979)
Increased activity on stabilimetric platform and in wheel running	Male rat (350-375)	915 (CW)	5	80 x 480	2.5	D'Andrea *et al*. (1980)

(continued)

TABLE 5-13. (continued)

Effects	Species (Weight, g)	Exposure Conditions Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR* (W/kg)	Reference
Decreased time on treadmill and inclined rod, decreased exploratory activity, increased then decreased shock sensitivity. Decreased activity and shock sensitivity persisted 90 days after exposure	Male rat	2375 (CW)	0.5	30 x 420	0.1	Rudnev et al. (1978)
Rectal temperature rise = 0.37 °C before start of test, ΔT = 1.5 °C with microwaves	Female rat	2450 (PW, multi-modal cavity, 60 and 12 Hz AM)		10 x 0.17 10 x 0.5	420 220	Bermant et al. (1979)
Response decreased during exposure on random interval schedule (lowest intensity for effect, ΔT = 1.8 °C)	Male rat (350-380)	500 (CW)	25	1 x 11	10	D'Andrea et al. (1976)
Response decreased during exposure (maximum effect) on random interval schedule, ΔT = 1.8 °C	Male rat (357-382)	600 (CW)	10	1 x 55	7.5	D'Andrea et al. (1977)
Decreased observing responses on vigilance task, ΔT = 2 °C	Male rhesus monkey (4 kg)	2450 (120 Hz, AM)	72	1 x 60	5.0	de Lorge (1976)
No effect on observing responses			16	1 x 20	1.1	
Decreased observing responses on vigilance task	Male squirrel monkeys (850-950)	2450 (120 Hz, AM)	50	1 x 30 1 x 60	2.8	de Lorge (1979)
No effect on observing responses				1 x 60	0.6-1.7	

(continued)

TABLE 5-13. (continued)

Effects	Species (Weight, g)	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR* (W/kg)	
Decreased observing responses on vigilance task	Male rat (362-400)	1280 (PW) 5620 (PW)	10 26	1 x 40 1 x 40	2.5 4.9	de Lorge and Ezell (1980)
Response rate decreased on fixed interval schedule in rats with high baseline rates, spending time away from lever	Male rat (290-340)	2450 (120 Hz, AM)	37.5	1 x 60	7.5	Sanza and de Lorge (1977)
No effect on response rate			8.8-18.4	1 x 60	1.8-3.7	
No effect on visual tracking task	Male rhesus monkey (6.2-7.9 kg)	1200 (CW)	20	1 x 120	1.6	Scholl and Allen (1979)
Response rate decreased on FR and increased on DRL schedules	Male rat (120 days, 150?)	2450 (CW) 2860 (PW) 9600 (PW)	5 5 5	1 x 30 1 x 30 1 x 30	1.4 1.4 1.5	Thomas et al. (1975)
Decreased length of runs and fewer reinforcers on FCN schedule	Male rat (250-300)	2450 (PW)	5	1 x 30	?	Thomas et al. (1976)
Decreased response rate on FR operant schedule	Male rat (284-439)	2450 (CW)	10	1 x 900	2.7	Gage (1979a)
Increased rate of missed observing responses on vigilance task	Young male rat	2450 (PW, AM, multimodal cavity)		1 x 30	6.5	Hunt et al. (1975)
Decreased rate of responding on repeated acquisition task	Male rat (275)	2800 (PW)	5	1 x 30	0.7	Schrot et al. (1980)

(continued)

TABLE 5-13. (continued)

Effects	Species (Weight, g)	Exposure Conditions Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR* (W/kg)	Reference
Increased response rates in extinction, decreased stimulus control, no effect on Sidman avoidance	Female rat	2450 (CW, multimodal cavity)	10	110 x 300	2.3	Mitchell et al. (1977)
No effect on flavor aversion test	Male rat (360-410)	918 (CW)	10	21 x 600	3.9	Moe et al. (1976)
No effect on flavor aversion test	Male rat (316-388)	918 (CW)	2.5	91 x 600	1.0	Lovely et al. (1977)
Microwaves detected as stimulus	Male rat (409-427)	2450 (PW, 120 Hz, AM, multimodal cavity)		1 x 1	0.6-2.4	King et al. (1971)
Microwaves detected as stimulus	Male rat (300-350)	918 (PW)	15	1 x 0.5	7.5	Johnson et al. (1976)
Spending more time in shielded vs. unshielded compartment	Female rat	1200 (PW)	0.2	4 x 30	0.2	Frey et al. (1975)
Spending equal time in shielded vs. unshielded compartment	Female rat	1200 (CW)	2.4	3 x 30	2.2	Frey et al. (1975)
Spending more time in shielded vs. unshielded compartment (occurred in first of 7 sessions)	Male rat (250)	1200 (PW)	0.4	1 x 90	0.4	Frey and Feld (1975)
Spending more time in unirradiated compartment	Male rat	2880 (PW)	9.5	9 x 60	2.1	Hjeresen et al. (1979)

(continued)

TABLE 5-13. (continued)

Effects	Species (Weight, g)	Exposure Conditions Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR* (W/kg)	Reference
Decrease in SAR at 24 °C	Male mouse (30-34)	2450 (CW)		1 x 15	28	Monahan and Ho (1976)
Decrease in SAR when ambient temperature increased from 20 °C to 35 °C	Male mouse (30-34)	2450 (CW)		1 x 20	43.6-0.6	Monahan and Ho (1977)
No preferential orientation of rats or mice in far field of plane wave	Male rat (200-360)	2450 (CW)	15	1 x 50	3.3	Gage et al. (1979)
	Male mouse (25-33)	2450 (CW)	15	1 x 60	6.2-12.3 (depending on orientation)	
Cannot take specific action to reduce intensity of irradiation	Female rat (290)	918 (PW, 60 Hz, AM, multimodal cavity)		5 x 2	60	Carroll et al. (1980)
Augmentation of increased response rates produced by chlordiazepoxide	Male rat (325-375)	2450 (PW)	1	1 x 30	0.2	Thomas et al. (1979)
Shift to left of dose-response curve for d-amphetamine in DRL schedule	Male rat (250-300)	2450 (PW)	1 1	1 x 30 4 x 30	0.2 0.2	Thomas and Maitland (1979)
No effect on dose response curve for chlorpromazine or diazepam	Male rat (360-380)	3800 (PW)	1	1 x 30	0.2	Thomas et al. (1980)

(continued)

TABLE 5-13. (continued)

Effects	Species (Weight, g)	Exposure Conditions Frequency (MHz)	 Intensity (mW/cm^2)	 Duration (days x min)	 SAR* (W/kg)	Reference
Chlordiazepoxide reduced responses, decreased avoidance responses, and increased escape responses to microwaves	Male mouse (35-44)	2450 (CW)		1 x 30	46	Monahan and Henton (1979)
Increased temperature during exposure caused greater response rate decreases after exposure	Male rat (315-365)	2450 (CW)	10	1 x 930	2.0	Gage (1979b)
Reduced responding for heatlamp in a cold room	Male rat 325-450)	2450 (CW)	5	1 x 15	1.0	Stern _et_ _al_. (1979)
Selection of a lower ambient air temperature	Squirrel monkey (750-1100)	2450 (CW)	6	1 x 10	1.0	Adair and Adams (1980b)

*If measured SAR was not reported, SAR was estimated when possible.

There is no unifying hypothesis to explain all the observed behavioral changes. The research on interaction between microwaves and chemicals has not been verified in independent laboratories, and it has not been extended to see if the interaction is limited to particular classes of compounds. Delineation of differences between effects of single and multiple exposures would help determine if effects of chronic exposure are qualitatively different from repeated measurement of effects of each single exposure.

Behavioral experiments have used only a limited sample of microwave exposure conditions. Exploration of frequency spectrum, modulations, waveforms, and interactions between waves of different parameters has hardly begun. Most behavioral work has used rats as subjects. Animals more like humans in physical size and shape have only infrequently been studied to help extrapolate findings to humans. Specifications of conditions of exposure other than the microwave stimulus such as ambient temperature and humidity have not been consistently controlled and reported so that their influence on behavior may be determined. There is no information on exposure effects of specific or limited areas of the body in comparison to total body exposure to evaluate the effects of localized energy absorption.

5.6 SPECIAL SENSES

Joe A. Elder

5.6.1 Cataractogenic Effects

A cataract is an opacity in the crystalline lens of the eye. These lens defects may be clinically insignificant or may cause partial or total blindness. The following conclusions may be drawn from animal experiments on the cataractogenic potential of RF radiation (Tables 5-14 and 5-15):

1. High-intensity RF radiation is cataractogenic.
2. For single acute exposures, the threshold intensity for cataract production exceeds 100 mW/cm^2. Multiple exposures at intensities near threshold values for single acute exposures will result in lens opacities.
3. The cataractogenic potential of RF radiation varies with frequency; the most effective frequencies appear to be microwave frequences in the 1-to 10-GHz range.
4. Similar ocular effects are produced by CW and PW radiation of the same average intensity.
5. In contrast with the above conclusions, which are based on acute, near-field exposures to the eye or head, no cataracts have been reported in unrestrained animals after far-field exposure at power densities near lethal values.

5.6.1.1 Microwave Radiation in Experimental Cataractogenesis--

The rabbit eye has been the experimental model most often used in animal studies because of its similarity in size and anatomy to the human eye (Figure 5-3). Its diameter is ~ 75 percent that of the human eye; the cornea is as large, and although the lens is thicker, its diameter is the same

TABLE 5-14. SUMMARY OF STUDIES CONCERNING OCULAR EFFECTS OF NEAR-FIELD EXPOSURES

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Cataract	Rabbit	5500 (CW and PW)	470-785*	1 x 2-100	300-500†	Birenbaum et al. (1969a)
Cataract	Rabbit	800 (CW) 4200 (PW) 4600 (PW) 5200 (PW) 5400 (CW and PW) 5500 (CW and PW) 6300 (PW)	785* 785* 785* 500-785* 500-785* 500-785* 785*	1 x 25 1 x 17 1 x 15 1 x 5-12 1 x 3-4 1 x 2-3 1 x 5	500† 500† 500† 350-500† 300-500† 300-500† 500†	Birenbaum et al. (1969b)
Cataract	Rabbit	2450 (CW)	180 120-180	1 x 240 20 x 60		Carpenter (1979)
No cataract	Rabbit	2450 (CW)	75	20 x 60		Carpenter (1979)
Cataract	Rabbit	2450 (CW)	150	1 x 100	138‡	Guy et al. (1975a)
Cataract	Rabbit	2450 (CW) 10,000 (CW)	295 375	1 x 30 1 x 30		Hagan and Carpenter (1976)
No cataract; keratitis (inflammation of cornea)	Rabbit	35,000 107,000	~ 40 ~ 40	1 x 60 1 x 60	> 175# > 238#	Rosenthal et al. (1976)

*Estimate calculated by dividing the microwave power by the irradiated area (d = 1.27 cm) of the eye.
†Estimate based on the assumption that all the incident power was absorbed by the eye (2 g).
‡Maximum SAR in the eye.
#Estimated SAR values for the cornea. (See text for discussion of Rosenthal et al. studies of frequency specificity.)

TABLE 5-15. SUMMARY OF STUDIES CONCERNING OCULAR EFFECTS OF FAR-FIELD EXPOSURES

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
No ocular effects, including no lenticular changes	Rabbit	3000 (CW)	100, 200	1 x 15, 30	14, 28*	Appleton *et al*. (1975)
Acute ocular changes, e.g., hyperemia of lids and conjunctiva, meiosis, anterior chamber flare, engorgement of iris vessels, and periorbital cutaneous burns; no lenticular changes			300, 400, 500	1 x 15	42, 56* 70*	
Death			300 500	1 x 30 1 x 15	42* 70*	
No cataracts	Rabbit	385 (CW) 385 (CW) 468 (CW)†	60 30 60	10 x 15 10 x 90 10 x 20	48* 24* 8.1	Cogan *et al*. (1958)
No cataracts	Rabbit	2450 (CW)	10	5 x 480 (x 8-17 weeks)	1.5*	Ferri and Hagan (1976)
No ocular effects	Monkey (*M. mulatta*)	9310 (PW)	150	30-40 x 294-665‡		McAfee *et al*. (1979)

*Estimated average whole-body SAR values (Durney *et al*. 1978, Figure 31).

†Waveguide average whole-body exposure.

‡Total exposure time in minutes for the entire 30- to 40-day experimental period.

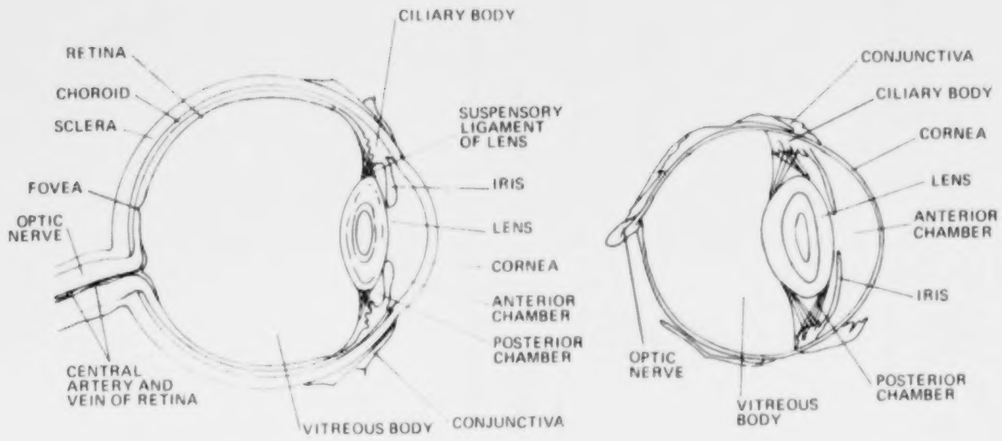
CILIARY BODY
RETINA
CHOROID
SCLERA
SUSPENSORY LIGAMENT OF LENS
FOVEA
IRIS
OPTIC NERVE
LENS
CORNEA
ANTERIOR CHAMBER
POSTERIOR CHAMBER
CENTRAL ARTERY AND VEIN OF RETINA
VITREOUS BODY
CONJUNCTIVA
CONJUNCTIVA
CILIARY BODY
CORNEA
LENS
ANTERIOR CHAMBER
IRIS
OPTIC NERVE
POSTERIOR CHAMBER
VITREOUS BODY

Figure 5-3. Cross-sectional sketch of the human (left) and the rabbit (right) eye (from Birenbaum et al. 1969a, Figure 1).

as that of the human eye. In a typical study (Carpenter et al. 1960b), one eye of an anesthetized rabbit was exposed to microwave radiation in the near field, and the nonirradiated eye served as the control. The eyes were then examined at various intervals using an ophthalmoscope, slit-lamp biomicroscope, or both instruments. The earliest positive reaction in this type of study, occurring within 24 to 48 h after a cataractogenic exposure, is the appearance of one or two narrow translucent or milky bands in the posterior cortex of the lens, just under the capsule, which extends no further than the lens equator. These bands can be seen only by slit-lamp examination with an angled beam. If the ocular injury is minimal, no further change occurs, and the cortical banding disappears within a few days. Otherwise, in 2 to 4 days after exposure small granules appear in the region of the suture of the posterior lens. If a more intense reaction occurs, larger numbers of granules appear over a larger area within the next few days, and small vesicles may develop. These early changes may develop further and become either well-defined circumscribed or diffuse cataracts. These lens changes remain as permanent ocular defects. In general, it has been found that microwave cataracts in rabbits involve only the posterior cortex of the lens, unless the exposure is so intense that the opacity extends throughout the lens.

At exposure levels that cause cataracts, other ocular reactions also occur, but these are transient and differ in severity with the intensity and duration of the exposure. Examples include swelling and chemosis of bulbar and palpebral conjuctivae, pupillary constriction, hyperemia of iris and limbal vessels, and vitreous floaters and filaments (Carpenter 1979).

5.6.1.2 Exposure Threshold Values for Cataracts--

Following the publication of reports demonstrating that microwaves can cause cataracts in experimental animals (Richardson _et al_. 1948; Daily _et al_. 1950a,b), three laboratories (Williams _et al_. 1955; Carpenter _et al_. 1960b; Carpenter and Van Ummersen 1968; and Guy _et al_. 1975a) published time vs. power-density threshold curves for cataract induction in rabbits by a single exposure to near-field 2.45-GHz radiation. The time vs. power-density threshold curves originally published by the three laboratories are similar in shape but are quantitatively different. The more recent studies found lower threshold values than those reported by Williams _et al_. (1955). This probably reflects differences in the irradiation method and in techniques used to measure power density. In fact, Carpenter (1979) has determined that his power densities were 50 percent higher than originally published. His corrected data are plotted in Figure 5-4 along with the results of Williams et al. (1955) for comparison. Guy et al. (1975a) replicated Carpenter's work for single acute exposures with essentially the same results, and also quantified the threshold of cataractogenesis in terms of SAR (see Figure 5-4). For example, these workers found the cataractogenic threshold for a 100-min exposure, the longest period of irradiation, to be 150 mW/cm^2 (138 W/kg) peak absorption (cf. Figure 5-5).

The cumulative effect of microwave radiation on cataractogenesis in the rabbit has been examined by repeatedly exposing the eye at power densities below the threshold for single acute exposures (Carpenter 1979). For example, daily 1-h exposures at 180 mW/cm^2 for 13 to 20 days were found to be cataractogenic in 8 of 10 animals, whereas single exposures at this power density were not effective. At 150 mW/cm^2, 4 of 10 rabbits gave a positive response after 18 to 32 daily exposures. No cataracts were observed after 20 daily 1-h exposures at 75 mW/cm^2.

If the entire body of an unanesthesized rabbit is exposed at power densities similar to those that cause cataracts under near-field conditions, the animal exhibits acute stress; Appleton et al. (1975) reported that rabbits became heat stressed and struggled out of the field during a 15-min exposure at 100 mW/cm^2. This report is described in more detail in § 5.6.1.5.

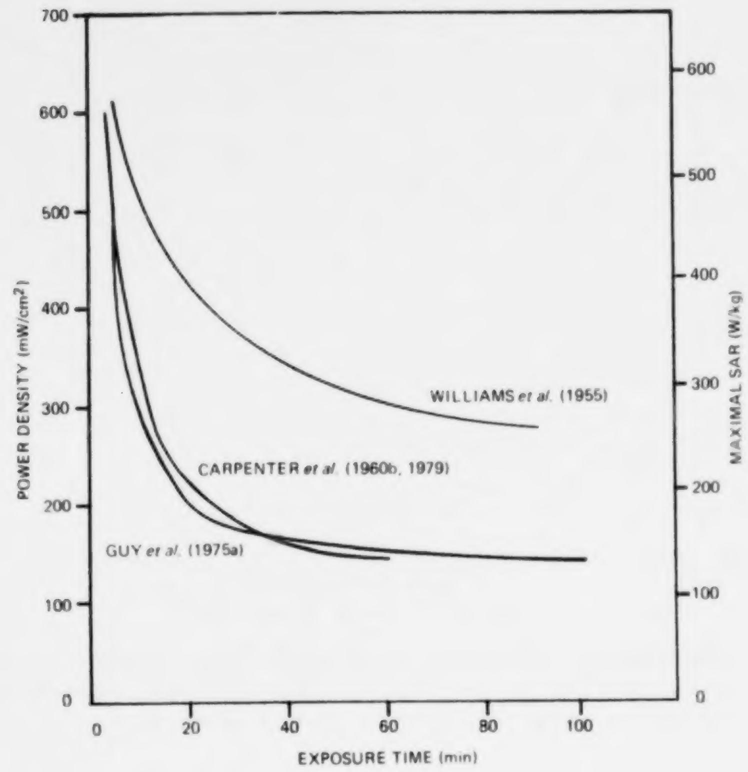

Figure 5-4. Time and power-density threshold for cataractogenesis in rabbits exposed to near-field 2450-MHz radiation; values of maximal SAR are also given (from Guy et al. 1975a, Figure 7).

5.6.1.3 Frequency Specificity--

As indicated above, most studies of experimental cataractogenesis were conducted at 2.45 GHz, but opacities in rabbit eyes have been reported after near-field exposures at 0.8, 4.2, 4.6, 5.2, 5.4, 5.5, 6.3, and 10 GHz (Birenbaum et al. 1969a,b; Hagan and Carpenter 1976). In several studies, the cataractogenic potential of different frequencies was addressed. For example, after Hagan and Carpenter (1976) determined the relative effects of 2.45- and 10-GHz (CW) radiation on the rabbit eye, they concluded that the cataractogenic potential

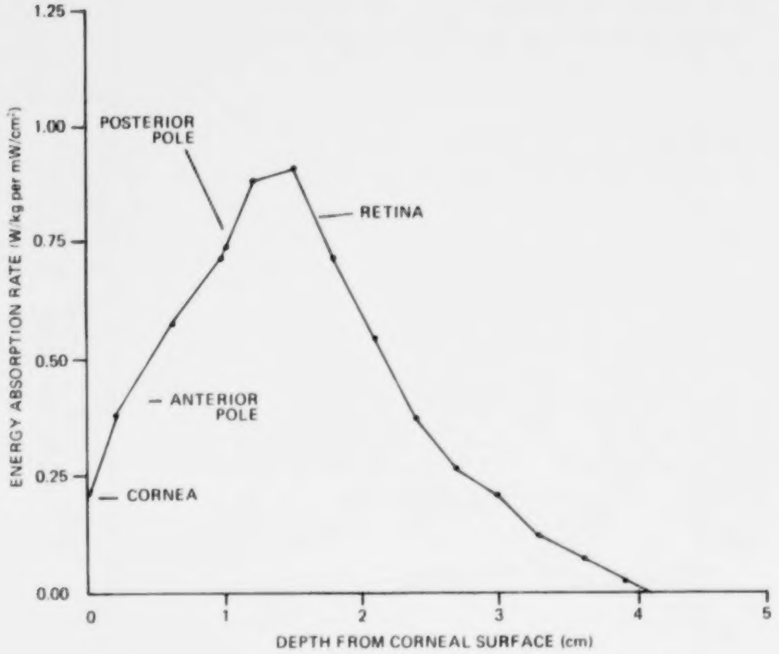

Figure 5-5. Distribution of energy absorption rate (W/kg) per mW/cm^2 incident power density in the rabbit's eye and head exposed to 2450-MHz radiation (from Guy et al. 1974, Figure 3).

for single acute exposures is greater at the lower frequency. At both frequencies, the opacities were characteristically located in the posterior subcapsular cortex of the lens, although the initial appearance and subsequent development differed. These differences probably reflect differences in the pattern of absorbed microwave energy in the eye due to the different depths of penetration of the radiation at these two frequencies.

Guy et al. (1974, 1975a) measured the distribution of absorbed energy in rabbit eyes exposed to 918- and 2450-MHz radiation and found the patterns to be significantly different. At 2450 MHz, energy absorption was maximal in the vitreous body at a point midway between the posterior surface of the lens and the retinal surface (Figure 5-5). The locus of peak absorption thus correlates well with the observation of irreversible changes in the posterior cortical lens. Exposure to 918-MHz fields in a specially devised cavity resulted in relatively uniform absorption in the eye, but maximal absorption was only ~ 25 percent of the peak absorption at 2450 MHz (Figure 5-6). Therefore, one would expect the threshold for cataractogenesis in rabbits exposed to 918 MHz to be considerably higher than the threshold at 2450 MHz. But more importantly, at 918 MHz, peak absorption in the rabbit brain was 36 percent higher than in the eye. It is possible that lens effects or ocular changes may not occur before more severe damage occurs in other sensitive tissues, such as the brain, during exposure to 918-MHz fields.

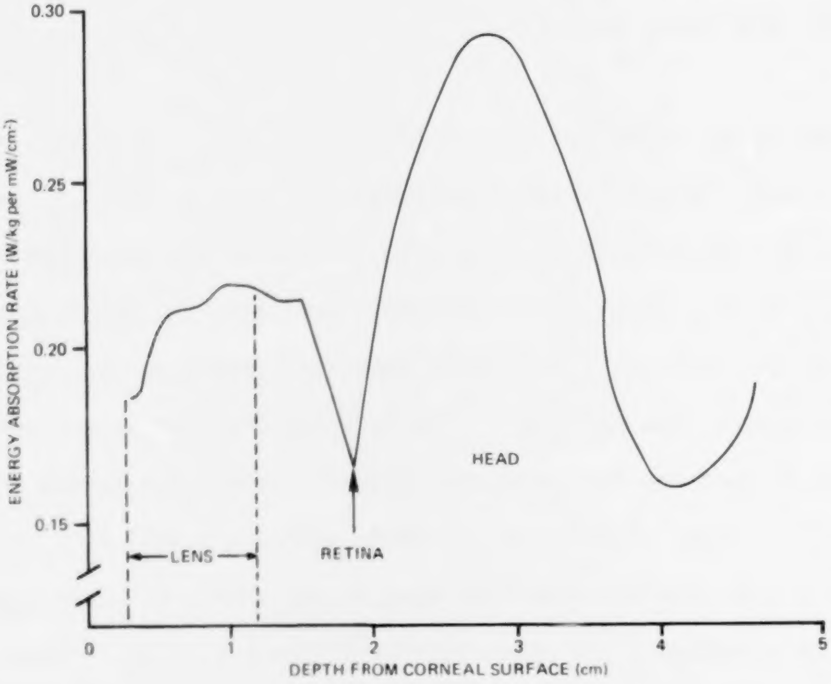

Figure 5-6. Distribution of energy absorption rate (W/kg) per mW/cm^2 incident power density in rabbit's head and eye exposed to 918-MHz radiation (from Guy et al. 1974, Figure 27).

Both Hagan and Carpenter (1976) and Guy _et al_. (1975a) used exposure systems that applied microwave energy across an air space to the eye, and both reported lenticular cataracts in the posterior subcapsular cortex. Birenbaum _et al_. (1969b) produced cataracts in the anterior cortex of rabbit lens with an exposure system that applied PW microwaves to the corneal surface. Furthermore, as the frequency decreased from 6.3 to 5.2 to 4.6 to 4.2 GHz, longer exposure times at a constant field strength were required to produce lens defects. Under similar experimental conditions, even longer exposure times were required to induce cataracts at a lower frequency, i.e., 0.8 GHz (CW) radiation. Furthermore, Birenbaum _et al_. (1969a) found no substantial difference in the cataractogenic threshold values for CW and PW 5.5-GHz radiation and concluded that the average, not the peak, rate of energy absorption determines whether lens injury will occur.

Rosenthal _et al_. (1976) examined the effects of 35- and 107-GHz radiation on the rabbit eye. At both frequencies keratitis (inflammation of the cornea) occurred at lower intensities than required to produce any other demonstrable ocular effect, such as lens injury (cataract) or iritis. Irradiation at 107 GHz was more effective in producing immediate corneal damage, but this change was generally gone by the next day. Effects at 35 GHz were persistent, were almost always present the next day, and were associated with marked injury to the corneal epithelium. Effects on the cornea correlate well with the pattern of microwave-energy absorption because most of the energy at these high frequencies is absorbed in the outer regions of the eye. The earliest stage of keratitis or minimal corneal stromal injury occurred after a 30-min exposure at an incident power of 50 mW or after a 60-min exposure at 25 mW. Estimates of the rate of energy absorption in the eye at the lower incident power (25 mW) are 35 mW at 35 GHz and 47.5 mW at 107 GHz (Rosenthal et al. 1976); therefore, the average SAR's of a rabbit eye weighing 2 g are 17.5 and 23.8 W/kg, respectively. Since maximal absorption occurs in the outer structures of the eye, the SAR in the cornea is estimated to exceed the average SAR of the eye by more than one order of magnitude.

Although the above data cannot be compared directly because of widely varying experimental procedures, these results indicate that the potential for cataract induction in rabbits is higher in the frequency range between 1 and 10 GHz than at either lower or higher microwave frequencies. Power densities that would cause cataracts at frequencies below 1 GHz and above 10 GHz give rise to insult in other ocular sites and extra-ocular tissues. Rosenthal et al. (1976) found that 35- and 107-GHz radiation primarily affected the outer structure of the eye, for example, the cornea; and at 918 MHz, Guy et al. (1974) showed that maximal energy absorption occurred in the brain, not in the eye.

The effects of near-field microwave exposures on the rabbit eye have been summarized by Cleary (1980) as follows:

> "The induction of cataracts in experimental animals, principally New Zealand white rabbits, has been described by a number of investigators using a variety of microwave exposure modalities. Generally microwave field intensities necessary for cataract induction in the rabbit are such that acute whole body exposures would be lethal due to hyperthermia. Most cataract studies have, therefore, employed focused or near-zone fields which limit exposures to the head or eyes. Localized thermal trauma is still of such a magnitude to necessitate the use of general or local anesthesia. Corneal irrigation with physiological saline solutions have also been used to

> prevent corneal damage due to tissue dehydration during microwave exposure. Anesthesia and corneal irrigation, as well as air temperature and humidity, may significantly affect the temperature of ocular structures."

The experimental results strongly suggest that radiation-induced temperature elevation may be essential for the cataractogenic effect of microwaves. Additional evidence for this position has been provided by Kramar et al. (1975), who reported that rabbits kept under general hypothermia during irradiation at known cataractogenic levels of 2.45-GHz (near-field) radiation did not develop cataracts. This study is described more fully in § 5.6.2.

5.6.1.4 Far-field Exposure Studies--

In contrast with the acute, near-field exposures that can cause cataracts and other ocular effects, cataracts have not been produced in rabbits whose entire bodies were exposed to radiation in the far field (Table 5-15). Appleton et al. (1975) exposed anesthetized rabbits to far-field radiation at 3000 MHz for 15 or 30 min at 100 or 200 mW/cm^2. No ocular changes were observed during or immediately after exposure. Fourteen daily examinations and four weekly examinations, followed by monthly examinations for 1 year revealed no lenticular changes. During exposure at higher levels (300, 400 or 500 mW/cm^2 for 15 min) animals exhibited acute ocular changes consisting of hyperemia of lids and conjunctiva, meiosis, anterior chamber flare, engorgement of iris vessels, and periorbital cutaneous burns. Subsequent examinations revealed no morphologic lenticular abnormalities. The authors concluded that "It is noteworthy that one year after a single microwave exposure, sufficient in intensity to cause both thermal cutaneous and acute gross ocular effects, no lens changes or cataracts were observed." It is also noteworthy that these power levels and durations were well above the cutaneous sensation level, because unanesthetized animals became heat stressed and struggled out of the field during a 15-min exposure at 100 mW/cm^2. Exposures at 300 mW/cm^2 for 30 min or 500 mW/cm^2 for 15 min were lethal to some of the rabbits.

Ferri and Hagan (1976) exposed unanesthetized rabbits to 2450-MHz (CW) radiation in the far field at 10 mW/cm^2, 8 h/day, 5 days/week for 8 to 17 weeks. Weekly examinations of the eye showed no abnormal changes during the study, and no post-irradiation changes were observed during the following 3 months.

Cogan *et al*. (1958) found no cataracts in rabbits 4 weeks after exposure at 385 MHz; the rabbits were irradiated twice weekly for 5 weeks at 60 mW/cm^2 for 15 min or 30 mW/cm^2 for 90 min. Six weeks after exposure in a waveguide, no cataracts were observed in rabbits irradiated at 468 MHz, 60 mW/cm^2 (SAR = 8.1 W/kg), for 10 days (20 min daily). Although the authors reported that the exposure levels at both frequencies were near lethal values, the 8.1 W/kg SAR is considerably lower than the value other investigators have found to be sublethal to rabbits (see Table 5-15). The environmental conditions (temperature, airflow, etc.) within the waveguide were not given; therefore, one must assume that the ambient conditions were significantly different from normal values or that the measured SAR is in error.

McAfee *et al*. (1979) trained unfettered monkeys (*Macaca mulatta*) to expose their faces and eyes to 9.31-GHz (PW) radiation at 150 mW/cm^2 average power density. Over a period of about three months, the animals were irradiated for a total of 294 to 665 min during 30 to 40 daily sessions. No cataracts or corneal lesions were observed in these monkeys during a 1-year period following irradiation.

5.6.2 Unresolved Questions

Exposure of the rabbit eye to microwave radiation at sufficient power densities and durations causes an immediate increase in intra-ocular temperature, and, after a latent period of a few days, opacities develop in the posterior subcapsular cortex of the lens (Kramar *et al*. 1975). This sequence of events has led to the assumption that microwave-induced lens opacities are thermally caused. Several experiments have been designed to test directly the cause-and-effect relationship between temperature increase and cataract formation. Kramar *et al*. (1975) exposed rabbit eyes to cataractogenic levels of microwave radiation while the animal's body was submerged in cold water. By this means, microwave-induced intra-ocular temperature was limited to < 41 °C, and no lens opacities developed. In a later experiment, Kramar *et al*. (1976) used heated water to produce ocular and rectal temperatures characteristic of those in rabbits exposed to a cataractogenic level of microwaves. Although the vicinity of the lens was heated to temperatures above those known to be associated with microwave cataracts, no lens opacities were observed; however, the rate of ocular temperature rise was about one-tenth the rate of increase with microwaves. Kramar *et al*. (1976) concluded that a combination of a sharp temperature gradient and rapid rise in temperature following irradiation may be more traumatic to the lens than a critical temperature *per se*.

Carpenter _et_ _al_. (1977) reported no cataracts of the posterior cortex of the lens in rabbits after 6 weeks of treatment in which "the eye was heated at the same rate, to the same extent, and for an equal period of time as it would experience during a cataractogenic microwave exposure, the difference being that the equal heating was provided by other means, namely, direct application of heat to the surface of the eye." In addition, elevating retrolental and rectal temperatures to values characteristic of a cataractogenic microwave exposure, through a combination of restricted body heat loss and irradiation of one eye to power densities slightly below the cataractogenic threshold, produced cataracts in only 3 of 10 rabbits. According to their hypothesis, if cataracts were solely of thermal origin, all animals given the two treatments should have developed cataracts. Carpenter _et_ _al_. (1977), therefore, concluded that the increase in intra-ocular temperature occurring during microwave irradiation is not the sole causative factor in microwave cataractogenesis.

The reason for the apparent disagreement between the conclusions of Carpenter _et_ _al_. (1977) and Kramar _et_ _al_. (1976) probably rests with the difficulty of duplicating by nonmicrowave heating techniques the temporal and spatial temperature profiles induced by microwave irradiation of the eye. Note that the temperature at a single site in the eye was the basis for evidence of duplicating microwave heating of the eye at the same rate and to the same extent. Furthermore, even though retrolental and rectal temperatures characteristic of cataractogenic microwave exposures were produced, the overall effects on the rabbits were more traumatic than a near-field microwave exposure to one eye. Within 24 h after heated water was applied directly to the eye, almost all the eyes exhibited hemorrhage into the anterior cavity, so that observation of the lens became impossible. Only 21 of 32 rabbits survived the heat treatment. Of these, five developed lenticular cataracts of the anterior cortex, and only three developed cataracts of the posterior cortex of the lens that are characteristic of microwave-induced opacities (Carpenter et al. 1977).

As mentioned above, the difficulty of duplicating by nonmicrowave techniques the time-temperature profile of microwave energy absorption in the eye is probably responsible for the unsuccessful attempts to prove that an elevation of temperature is responsible for microwave cataracts (cf. Kramar et al. 1976; Carpenter et al. 1977). On the other hand, strong evidence for thermalization being the causative factor in microwave cataracts is provided by the experiment of Kramar et al. (1975), which showed that cataracts were not produced in hypothermic rabbits receiving a cataractogenic microwave exposure. At present, it is generally understood that intense localized exposure of the eye for substantial durations (i.e., 150 mW/cm^2 for 100 min) is necessary to induce cataracts in laboratory animals, and that such acute exposures cause death by hyperthermia if the entire animal is irradiated.

5.6.3 Auditory Effects

When the human head is exposed to PW RF radiation, an audible sound described as a click, buzz, chirp, or a knocking sensation is perceived by some individuals; the sound appears to originate from within or behind the head. This auditory phenomenon is called "RF sound" or "RF hearing." Our present knowledge of RF hearing is summarized below.

1. The RF sound occurs only upon exposure to PW sources; it appears to originate from within or near the back of the head regardless of orientation of the head in the RF field, and the sound varies with pulse width and pulse repetition rate.

2. The effective frequency range is 216 to 6500 MHz. The effect has been found to occur at average power densities as low as 0.001 mW/cm^2 with peak power densities in the range of 100 to 300 mW/cm^2. Effective pulse widths vary from 1 to 1000 μs. (See Table 5-16.)

3. The ability to perceive RF pulses has been shown to be related to bone-conduction hearing and to the ability to hear high frequency acoustic waves above 5 to 8 kHz.

4. The available data support the conclusion that the RF auditory effect is evoked by a mechanism similar to that for conventional acoustic stimuli and that the primary site of interaction is peripheral to the cochlea.

5. The most generally accepted mechanism responsible for the RF auditory sensation is thermoelastic expansion. That is, the absorption of the energy in a brief RF pulse causes a small temperature rise ($\sim 10^{-6}$ °C) in a short time (~ 10 μs), which results in thermoelastic expansion of matter within the head, which then launches an acoustic pressure wave that is detected by the hair cells in the cochlea via bone conduction.

5.6.3.1 Human Perception of Pulsed RF Radiation--

Frey (1961) was the first to study systematically the human auditory response to pulse-modulated radiation. The subjects, who were more than 30 m from an enclosed antenna, reported hearing a transient buzzing sound upon exposure to the intermittent rotating beam. The apparent location of the sound, which was described as a short distance behind the head, was the same no matter how the people were oriented in the RF field. When an RF shield (aluminum flyscreen) was placed between the subject and the RF source, the subject did not perceive RF sounds (Frey 1973). When earplugs were used, a reduction in the ambient noise level and an increase in the RF sound level were reported. The sensitive area for detecting RF sounds was later described

TABLE 5-16. SUMMARY OF STUDIES CONCERNING AUDITORY EFFECTS OF RF RADIATION IN HUMANS

		Exposure Conditions								
Effect	Comment	Number of Subjects	Frequency (MHz)	Pulse Repetition Rate (s^{-1})	Pulse Width (μs)	Peak Intensity (mW/cm^2)	Average Intensity (mW/cm^2)	Energy/ Pulse (J/cm^2)	Noise Level (dB)	References
RF hearing "distinct" clicks"	Threshold values	8	3000	0.5	5 10 15	2500 225-2000 300-1000	0.006 0.001-0.01 0.002-0.007	12.5 2.3-20.0 4.5-15.0	45 (+ plastic foam ear muffs)	Cain and Rissmann (1978)
RF hearing: buzz heard at PRR > 100; individual pulses heard at PRR < 100		3	3000	<100-1000	1-2	2500-50,000	5	40		Constant (1967)
			6500	<100-1000	1-2	2500-50,000	5			
No auditory response			9500		0.5					Constant (1967)
RF hearing "buzzing sound"		4	1245 1245	50 50	10 70	370 90	0.19 0.32			Frey and Messenger (1973)
RF hearing "buzz, clicking, hiss, or knocking"	Threshold values	Not given	216 425 425 425 425	- 27 27 27 27	- 125 250 500 1000	670 263 271 229 254	4.0 1.0 1.9 3.2 7.1		70-90 (+ ear stopples)	Frey (1962, 1963)
No auditory response			8900	400	2.5	25,000	25		70-90 (+ ear stopples)	Frey (1962)
RF hearing "buzzing sound"	Threshold values	8 7	1310 2982	244 400	6 1	267 5000	0.4 2		70-80 (+ ear plugs)	Frey (1961)
RF hearing "clicks, chirps"	Threshold values	1	2450	3	1-32	1250-40,000	0.1	40*	45	Guy et al. (1975)
RF hearing	Polytonal sound	18	800	1000-1200	10-30	> 500	-	-	40 (+ ear (stopples)	Tyazhelov et al. (1979b)

*Calculated peak-absorbed-energy-density per pulse is 16 mJ/Kg.

as a region over the temporal lobe of the brain, because the placement of a small piece of metal screen (5 x 5 cm) over this area completely stopped the RF sound (Frey 1962).

Guy _et al_. (1975b) described the effect of PW radiation on two of the coinvestigators. Three pulses, 100 ms apart, were presented each second to keep the average power density below 1 mW/cm^2. Each individual pulse was heard as a distinct and separate click, and short pulse trains were heard as chirps with the tone corresponding to the pulse repetition rate (PRR). The RF sound appeared to originate from within or near the back of the head. This report also included the note that transmitted digital codes could be accurately interpreted by the subject when the pulse generator was keyed manually. Guy _et al_. (1975b) also reported that the threshold for RF hearing was lower when ear plugs were used.

In a study by Constant (1967), the RF sound was described as being in the area of the ear on the side opposite to the one that was irradiated. All three of his subjects readily detected 2-μs pulses, whereas 0.5-μs pulses were not perceived. All three experienced a buzzing sensation at PRR's greater than 100/s, whereas individual pulses were heard when subjects were exposed to PRR's below 100/s.

Five of eight human subjects reported hearing distinct clicks either inside the head or behind the head when exposed to 15-μs pulses (Cain and Rissmann 1978). The remaining three people heard faint clicks when the pulse width was increased to 20 μs.

5.6.3.2 Effective Radiation Parameters--

In the initial report by Frey (1961), human subjects perceived PW radiation at frequencies of 1310 and 2982 MHz. Although the peak of power-density thresholds for RF hearing was 266 mW/cm^2 for 1310-MHz and 5000 mW/cm^2 for 2982-MHz fields, the average power density thresholds were 0.4 mW/cm^2 and 2 mW/cm^2, respectively. When ear plugs were used to attenuate the ambient noise level of 70 to 80 dB, the subjects reported an increase in the RF sound levels.

In the following year, Frey (1962) reported that humans could perceive PW radiation at 425 MHz with an average power density threshold of 1 mW/cm^2; the peak of power density was 263 mW/cm^2. A frequency of 8900 MHz was not effective even at an average power density of 25 mW/cm^2; the peak of power density was 25,000 mW/cm^2. At 216 MHz, the lowest effective frequency reported in the literature, the average power density threshold was 4 mW/cm^2; the peak of power density was 670 mW/cm^2 (Frey 1963). Later, in a study of four subjects exposed to 1245-MHz PW radiation, Frey and Messenger (1973) concluded that perception was dependent primarily upon peak power and secondarily upon pulse width. They reported that the peak power for perception was somewhat less than 80 mW/cm^2 for pulse widths of 10 to 70 μs.

In the study by Constant (1967), three human observers were exposed to PW radiation at 3, 6.5, and 9.5 GHz at an average power density of 5 mW/cm^2 (pulse width was 0.5 to 2.0 μs; PRR was up to 1000/s). Only two of the three observers perceived 3- and 6.5-GHz radiation; none experienced a response to the highest frequency. Cain and Rissmann (1978) reported that all eight of their subjects heard RF pulses at 3 GHz. In this study, plastic foam earmuffs were worn to attenuate the ambient noise, which was 45 dB. The average threshold energy density per pulse was 10.6 μJ/cm^2 (range of values was 3.4 to 17.5 μJ/cm^2).

The range of microwave pulse widths varied from 1 to 32 μs in the study by Guy et al. (1975b) on one human subject. The results indicate that regardless of the peak power of the pulse or the pulse width, the threshold for RF hearing of 2450-MHz radiation was related to an energy density of 40 μJ/cm^2 per pulse, or energy absorption per pulse of 16 μJ/g, as calculated with the aid of a spherical model. The background noise of the exposure chamber was 45 dB. When earplugs were used, the threshold level decreased to 28 μJ/cm^2. The threshold for a second subject, who had a hearing deficit, was approximately 135 μJ/cm^2. Guy et al. (1975b) stated that two pulses which occurred within several hundred microseconds of each other were perceived as a single pulse with energy equal to the sum of the two pulses.

The human studies cited above indicate that the highest effective frequency of RF hearing is between 6.5 and 8.9 GHz and that the lowest effective frequency is 216 MHz. Also, the results describe other radiation parameters (peak power density, energy density per pulse, and pulse width) that are important in determining the threshold for RF hearing in humans.

5.6.3.3 Dependence of RF Hearing on Acoustic Hearing--

Standard audiograms measure hearing thresholds for air conduction at acoustic frequencies of 250 to 8000 Hz and for bone conduction to 4000 Hz. Cain and Rissman (1978) measured the hearing ability of eight subjects over the frequency range of 1 to 20 kHz in addition to determining their standard audiograms. They found that, although there was no apparent correlation between the ability to perceive pulsed microwaves at 3000 MHz and hearing ability as measured by standard audiograms, there was a strong correlation between microwave-hearing threshold and hearing thresholds to air-conducted acoustic signals above 8 kHz. For example, three of the subjects who had normal hearing below 4 kHz could not hear microwave pulses of less than 20-μs duration under conditions in which the other subjects could perceive RF sounds. All three had a hearing deficit at frequencies above 8 kHz.

Frey (1961) compared human acoustical hearing and RF hearing and reported that a necessary condition for perceiving the RF sound was the ability to hear audiofrequencies above approximately 5 kHz, although not necessarily by air conduction. This conclusion was based on one subject who had normal air-conduction hearing but failed to hear the microwave pulses. The person was subsequently found to have a substantial loss in bone-conduction hearing. On the other hand, a subject with good bone-conduction hearing but with poor air-conduction hearing perceived the RF sound at approximately the same power density that induced threshold perception in subjects with normal hearing. The studies by Cain and Rissmann (1978) and by Frey (1961) show RF hearing to be dependent on high-frequency hearing above 8 kHz and bone-conduction hearing at lower acoustic frequencies.

5.6.3.4 Similarity of Auditory Response to Microwave and Conventional Acoustic Stimuli--

Taylor and Ashleman (1974) measured the electrical response in three successive levels of the cat auditory nervous system (eighth cranial nerve, medial geniculate nucleus, and primary auditory cortex) to both acoustic and pulsed-microwave (2450-MHz) stimuli. They concluded that the microwave-induced auditory effect on the animal is exerted similarly to that of conventional acoustic stimuli. Furthermore, these authors reported that inactivation (perforation of the round window and aspiration of perilymph) of the cochlea, the known first stage of transduction for acoustic stimuli, affected the central nervous system (CNS) response to acoustic and microwave energy in the same way; i.e., the evoked electrical activities of all three sites were abolished by cochlear destruction. These results indicated that the locus of the initial interaction of pulse-modulated microwave energy with the auditory system might reside peripheral to the cochlea.

In an experiment in which the thresholds of evoked electrical responses from the medial-geniculate body in cats were determined as a function of background noise, Guy et al. (1975b) found that as the noise level (50 to 15,000-Hz bandwidth) increased from 60 to 80 dB, there was only a negligible increase in the threshold for the 2450-MHz microwave stimuli, a moderate increase in the threshold for a piezoelectric bone-conduction source, and a large increase in the threshold for loudspeaker-produced stimuli. The finding that the evoked response to microwave stimuli did not increase in relation to background noise, which included acoustic frequencies to 15,000 Hz, indicates that microwaves may interact with the high-frequency portion of the auditory system.

Guy et al. (1975b) also demonstrated that potentials evoked by microwave stimuli could be recorded at CNS sites other than those that correspond to the auditory nervous system. This finding indicates that elicited potentials recorded from any CNS location could be misinterpreted as indicating a direct microwave interaction with the particular system in which the recording is made.

Prior to 1970, Frey (1962) had suggested that RF hearing might be a result of direct cortical or neural stimulation. He based this suggestion on (1) his observations that the perception of RF pulses was instantaneous and occurred at low average-incident-power densities and on (2) the failure to record cochlear microphonics at power densities much higher than those required to elicit auditory nerve responses. Cochlear microphonics are electrical potentials that mimic the sonic waveforms of acoustic stimuli; they are the signature of mechanical distortion of cochlear hair cells, the first stage of sound transduction. The failure to observe microwave-induced cochlear microphonics had led to the suggestion that pulsed microwaves, unlike conventional acoustic stimuli, may not act on any sensor prior to acting directly on the inner ear apparatus (Frey 1967).

In 1975, Chou et al. reported their success in overcoming the technical problems that had prevented investigators from recording cochlear microphonics from microwave-irradiated animals. The cochlear microphonics of guinea pigs exposed to 918-MHz (PW) radiation were found to be similar to those evoked by acoustic stimuli.

The results of the above studies of evoked electrical potentials in the auditory system, including the demonstration of pulsed-microwave-evoked cochlear microphonics, strongly indicate that the microwave-induced auditory sensation is detected similarly to conventional sound detection and that the site of conversion from microwave to acoustic energy resides peripheral to the cochlea. However, it is not known what structure(s) in the head transduce(s) the microwave energy to acoustic energy.

5.6.3.5 Mechanism of RF Hearing--

As mentioned above, Frey (1967) had suggested that RF hearing might be a result of direct cortical or neural stimulation because of the failure to record cochlear microphonics and because the perception of RF pulses was instantaneous and occurred at low average-incident-power densities. The latter points were evidence against a radiation-pressure/bone-conduction hypothesis (see also Guy et al. 1975b). Sommer and von Gierke (1964) had suggested that radiation pressure exerted by the RF pulse impinging on the surface of the head could launch an acoustic signal of sufficient amplitude to be detected by the inner ear via bone conduction. Other types of pressure much greater than radiation pressure can be produced in tissue exposed to RF pulses. These include thermal expansion forces that are proportional to the square of the electric field in the material. For example, Gournay (1966) has shown that pressures greatly exceeding radiation pressure result when visible light from a laser is converted to acoustic energy by thermal expansion due to absorbed energy in various liquids.

Foster and Finch (1974) extended Gournay's analysis to a physiological solution exposed to microwave pulses similar to those that produce RF hearing in humans. They showed both theoretically and experimentally that radiation-induced pressure changes would result from the absorption of RF pulses and could produce significant acoustic energy in the solution. In fact, audible sounds were produced by rapid thermal expansion, resulting from only a 5×10^{-6} °C temperature rise in the physiological solution, due to the absorption of the energy in the RF pulse. The authors concluded that the RF sounds involve perception, via bone conduction, of the thermally generated sound transients caused by the absorption of microwave pulses. The pulses must be moderately intense (typically 500 to 5000 mW/cm^2 at the surface of the head). However, they can be sufficiently brief ($\leq$ 50 μs) such that the maximum increase in tissue temperature after each pulse is very small ($< 10^{-5}$ °C)

The hypothesis of Foster and Finch (1974) predicts that the RF hearing effect is related to thermoelastically induced mechanical vibrations in the head. Vibrations of this type can be produced by other means such as a laser pulse or by a pulsed piezoelectric crystal in contact with the skull (Chou et al. 1976). Frey and Coren (1979) used a holographic technique to test whether the skull and the tissues of the head of an animal have the predicted vibrations when exposed to a pulsed RF field. No displacements were recorded, but, subsequent to this report, Chou et al. (1980) demonstrated that the sensitivity of the holographic technique used by Frey and Coren (1979) was three to four orders of magnitude too low to detect displacements related to vibrations from microwave-induced thermoelastic expansion in biological tissues.

Tyazhelov et al. (1979b) conducted a series of psychophysical experiments with 18 subjects to evaluate the adequacy of the thermoelastic hypothesis and to study the perceptual qualities of RF-induced sounds. Audiofrequency signals were presented alternately to or concurrently with microwave pulses (see Table 5-16) under conditions in which the subject could adjust the amplitude, frequency, and phase of the audio signal. The authors concluded that the thermoelastic hypothesis adequately explained some of their findings for microwave pulses of high peak power and short width (< 50 μs), but other results were interpreted as inconsistent with a thermoelastic mechanism for RF hearing. For example, pulse widths greater than 50 μs, which increased the mean power level, produced increases in loudness that rose more rapidly than predicted by the thermoacoustic model. In addition, suppression of RF sounds by the audio signal was reported to be inconsistent with the model.

Lebovitz and Seaman (1977) compared the response to pulsed microwaves (915 MHz) with the response to acoustic clicks by monitoring single auditory neurons in the cat. A response of these neurons to pulsed microwaves was predicted by earlier studies that demonstrated subjective auditory perception (Frey 1962), auditory evoked potentials (Taylor and Ashleman 1974), and cochlear microphonics (Chou et al. 1975). Furthermore, the thermoelastic model predicts that a mechanical wave of pressure stimulates the inner ear via bone conduction. Thus, the response of the neurons in the auditory pathway to pulsed microwaves should be similar to their response to transient mechanical stimuli such as acoustic clicks. The results indicated that mechanical factors within the cochlea are similarly involved in determining both the acoustic and the pulsed microwave response (Lebovitz and Seaman 1977).

Other data in this report (Lebovitz and Seaman 1977) appeared to be inconsistent with the thermoelastic model that predicts a high-frequency component such as the microwave-induced cochlear microphonic recorded by Chou et al. (1975). That is, Lebovitz and Seaman (1977) observed a decrease in sensitivity of high-frequency auditory units to microwave pulses. However, they used long pulses of 250 to 300 μs in duration to obtain maximal energy per pulse. More recently, Tyazhelov et al. (1979b) reported that long pulses (~ 100 μs) result in a lower pitch of the RF sound in humans. Two of their observers who had a high-frequency auditory limit of 10 kHz could not hear short RF pulses but could hear long pulses. Thus, the results of single unit recordings in cats are consistent with human perception of RF pulses when the pulse widths are long.

Lin (1977) developed a theoretical model that estimates the characteristics of acoustic signals induced in laboratory animals and humans by microwave pulses; his model is based on thermal expansion in spherical heads irradiated by pulsed microwave energy. The frequency of the induced sound was found to be a function of head size and of acoustic properties for brain tissues; hence, the acoustic pitch perceived by a given subject will be the same regardless of the RF frequency. The calculations of Lin show that the fundamental frequency predicted by the model varies inversely with the radius of the head; i.e., the larger the radius, the lower the frequency of the perceived RF sound. He estimated the fundamental frequency of vibration in guinea pigs, cats, and adult humans to be 45, 38, and 13 kHz, respectively. The frequency for an infant head was estimated to be about 18 kHz. These results appear to be in good agreement with the measurements of Chou et al. (1975), who found cochlear microphonics in guinea pigs to be 50 kHz. In addition, the calculations provide further evidence that a necessary condition for auditory perception by adult humans is the ability to hear sound above 5 to 8 kHz (Frey 1961, Rissmann and Cain 1975). However, the prediction that the pitch perceived by a given subject will be the same regardless of the RF frequency is not in agreement with the experimental finding that long pulses result in a lower pitch of the RF sound in humans (Tyazhelov et al. 1979b). Other unresolved questions are discussed below.

5.6.4 Unresolved Questions

Several investigators have tried to determine the thresholds for the RF-induced auditory sensation in human beings and in laboratory animals

(Table 5-17). Human studies and animal experiments, in general, are few and have used small sample sizes, different frequencies, and different experimental procedures. However, the radiation parameters that are most important in determining the threshold for the auditory response in humans (discussed in § 5.6.3.2, Effective Radiation Parameters) and in laboratory animals (discussed below) are being characterized.

The threshold for an auditory response in cats exposed to 918- and 2450-MHz (PW) radiation was studied by recording electric potentials from the medial geniculate body (Guy et al. 1975b). As the pulse width increased from 0.5 to 32 μs, the threshold value for the peak of power density decreased proportionately for pulse widths below 10 μs. The thresholds of average power density and energy density per pulse also increased with pulse width, but these parameters did not show the strong proportional relationship with pulse width as did the peak of power density. Guy et al. (1975b) concluded that the threshold for the evoked auditory response was related to the incident energy density per pulse, at least for pulse widths less than 10 μs. The threshold energy density per pulse was found to be about one-half of that which had produced a sensation in one human subject. Later, one of the coauthors (Lin 1978) stated that one cannot easily rule out the possible connection between the pulsed-microwave-evoked auditory responses and other radiation parameters, including peak incident power density, absorbed energy, and pulse width.

In a similar experiment conducted at frequencies between 8670 and 9160 MHz, Guy et al. (1975b) found that the threshold values of power density and of energy density per pulse, which include the auditory response of cats, were

TABLE 5-17. SUMMARY OF STUDIES CONCERNING THRESHOLD VALUES FOR AUDITORY-EVOKED POTENTIALS IN LABORATORY ANIMALS

Effect	Species (n)	Exposure Conditions Frequency (MHz)	Pulse Repetition Rate (s^{-1})	Pulse Width (μs)	Pulse Intensity (mW/cm^2)	Average Intensity (mW/cm^2)	Incident Energy Density Per Pulse ($\mu J/cm^2$)	Peak Absorbed Energy Density per Pulse (μJ/g)	References
Response obtained with scalp electrodes	Cat (2)	3000	0.5	5 10 15	2200,2800 1300 580		11,14 13 8.7		Cain and Rissmann (1978)
Response obtained from round window with carbon lead	Guinea pig (5)	918	100	1-10	*	*		20	Chou et al. (1975)
Response obtained from medial geniculate with glass electrode	Cat (2)	918 2450 8670-9160	1 1 1	3-32 0.5-32 32	800-5800 600-35600 14800-38800	0.017-0.028 0.015-0.047 0.472-1.24	17.4-28.3 15.2-47.0 472-1240	12.3-20.0 8.7-26.7	Guy et al. (1975b)
Response obtained from individual auditory neurons with glass electrode	Cat (not given)	915	< 10	25-250	-	≤ 1.0	-	4-40	Lebovitz and Seaman (1977)

*Direct comparison of power density in the waveguide exposure system to free-field power density is improper because the efficiency of energy coupling is ten times higher than for free-field exposure. (See Chou et al. 1975, p. 362.)

an order of magnitude higher than those required at 918 and 2450 MHz (Table 5-17). Furthermore, no auditory response was obtained at 8670 to 9160 MHz until the brain was exposed by enlarging the hole in the skull that served as the electrode access port.

Cain and Rissmann (1978) determined the threshold for auditory responses in animals exposed to 3000-MHz (PW) radiation. Although their results are in general agreement with Guy _et_ _al_. (1975b) in that the threshold energy density per pulse was relatively constant for pulse widths of 5, 10, and 15 μs, their results are confounded by the use of scalp electrodes and only few animals of three species (two cats, two chinchillas, and a dog).

Lin (1978) concluded that the studies on microwave-induced auditory sensations in laboratory animals strongly indicate a threshold, but the exact numerical value must await further experimentation. Furthermore, if the available threshold data are analyzed as a function of microwave frequency, it becomes clear, both in terms of the peak of power density and peak rate of energy absorption, that the threshold differs for different frequencies even in the same animals (Lin 1978).

Recently, Wilson _et_ _al_. (1980) described an autoradiographic technique using [^{14}C]2-deoxy-D-glucose to map auditory activity in the brain of rats exposed to acoustic stimuli and to PW and CW microwave radiation. With this technique, _in_ _vivo_ determination of metabolic activity, i.e., glucose utilization and associated functional activity in the brain, can be visualized.

Prior to exposure to the acoustic stimuli or to microwaves, one middle ear was ablated. First, the authors showed the expected bilateral asymmetry of radioactive tracer uptake in the auditory system of rats exposed to acoustic clicks or weak background noise. Second, in contrast, a symmetrical uptake of tracer was found in animals exposed to PW radiation. Thus, the autoradiographic results confirmed the finding that RF hearing does not involve the middle ear (Frey 1961; Chou and Galambos 1979). Unexpectedly, Wilson et al. (1980) found similar patterns of radioactive tracer uptake in the auditory system of rats exposed to CW radiation (918 MHz; 2.5 and 10 mW/cm^2) and to PW radiation (2450 MHz). This result, indicating an auditory response to CW microwaves, was unexpected, because no report of a direct hearing sensation due to exposure to CW microwaves had appeared in the literature. Since the thermoelastic hypothesis of RF hearing is based on the properties of PW radiation, this observation suggests that another mechanism may be involved in the interaction of RF radiation with the auditory system of the brain.

5.6.5 Human Cutaneous Perception

Exposure of the human body to microwave radiation can cause heating that is detectable by the temperature sensitive receptors in the skin. As shown in Table 5-18, several investigators have experimentally determined the microwave intensities that cause sensations of warmth and pain in human subjects.

5.6.5.1 Frequency Specificity--

Hendler and colleagues (1963, 1968) exposed a circular area (37 cm^2) of the forehead to 3- and 10-GHz (PW) radiation and to infrared (IR) radiation.

TABLE 5-18. SUMMARY OF STUDIES CONCERNING HUMAN CUTANEOUS PERCEPTION OF RF RADIATION

Effect	Frequency (MHz)	Intensity (mW/cm^2)	Duration (s)	SAR* (W/kg)	Reference
Sensation of warmth on forehead	3000 (PW)	-	1-5	20-40	Hendler (1968)
	10,000 (PW)	-	1-5	25-35	Hendler _et_ _al_. (1963)
Sensation of warmth on forehead	2880	74 56	15-73 50-180	- -	Schwan _et_ _al_. (1966)
Sensation of warmth on inner forearm	3000 (PW)	300-2500	$\leq$ 6	-	Vendrick and Vos (1958)
Sensation of pain on inner forearm	3000	2500 1000	30 130	2000	Cook (1952)

*SAR value is estimated.

The forehead was selected for a study of warmth sensations because the temperature receptors in the skin of the forehead are relatively numerous and are evenly distributed, so that the area constitutes a low-threshold region of uniform temperature sensitivity. The lower-frequency microwaves (3 GHz) had a higher intensity threshold for warmth sensation. The higher-frequency IR radiation was more effective than either microwave frequency, because the IR energy was absorbed more effectively in the outer skin layers containing the thermal sensors.

5.6.5.2 Temperature Thresholds--

For both microwave and IR radiation at intensities producing warmth sensations, a threshold of warmth was experienced when the temperature of a more superficial layer of subcutaneous tissue ~ 0.2 mm below the skin's surface was increased ~ 0.01 to 0.02 °C over the temperature of a deeper layer in the skin lying ~ 1 mm below the surface. In this study it was also noted that there was a persistent sensation of warmth for ~ 7 s after cessation of the exposure, which indicated the continued existence of an effective temperature difference between the subcutaneous tissue layers (Hendler 1968).

Schwan *et al*. (1966) exposed a small area of the forehead (7-cm diameter) equivalent to the area exposed in Hendler's studies to 2.88-GHz radiation and measured the length of time that elapsed before the person was aware of a sensation of warmth. The times for four subjects varied from 15 to 73 s at 74 mW/cm^2 and from 50 to 180 s at 56 mW/cm^2. The authors found that the reaction times were not linearly proportional to the reciprocal of the incident power density and concluded that subjective awareness of warmth was not a reliable indication of microwave hazard.

Vendrik and Vos (1958) exposed a 13-cm^2 area of the inner forearm to 3-GHz (PW) radiation (300 to 2500 mW/cm^2) and found the threshold for temperature changes to be 0.4 to 1.0 °C. Skin temperature increases that were kept below 1 °C were linear with microwave intensity for six exposure durations. In contrast to the regularity of skin temperature changes induced by microwaves, the reports of temperature sensations were variable. Sensations of warmth occurred < 0.5 to 3.5 s after rapid rises in skin temperature. The sensations did not cease when the skin temperature began to drop. In this study, microwave radiation (3 GHz) was found to be a factor of 10 less effective in producing a temperature elevation than was IR radiation at a similar intensity.

Cook (1952) determined the pain threshold in six subjects who were exposed to 3-GHz radiation at five different sites on the body's surface. The initial skin temperature ranged from 31.5 to 33.5 °C. Pain resulted when a critical skin temperature (~ 46 °C) was reached rather than from a critical temperature rise (ΔT). For an inner forearm area of 9.5 cm^2, the power density pain thresholds varied from 2500 mW/cm^2 for a 30-s exposure to 1000 mW/cm^2 for an exposure of 130 s. The pain threshold was lower for a larger exposed area of 53 cm^2. The skin temperature corresponding to burning pain was found to be independent of the area of exposure, radiation intensity, exposure time, and anatomical site. At high intensities, the exposure time needed to produce pain was an inverse function of radiation intensity. The author reported that the sensations of warmth and pain with microwave heating differed little from those resulting from IR radiation.

5.6.6 Unresolved Questions

The few studies on pain and warmth sensations in human beings exposed to frequencies in the range of 3 to 10 GHz provide useful data on exposure levels that are clearly undesirable for the general population. Cutaneous perception, however, may be a reliable indicator of an unsafe exposure level only at RF frequencies with wavelengths small in comparison to the length of the exposed body, i.e., wavelengths comparable to or smaller than the thickness of skin. Under these conditions, most of the energy is absorbed in the outer tissue layers containing thermal sensors. At lower frequencies, which have wavelengths approximately equal to or longer than the human body, modeling studies have shown that much of the energy is absorbed within the body below the superficial skin layers. One should make note of the fact that, in all mammals tested, the threshold temperature (~ 42 °C) of cellular injury for sustained elevations (seconds to tens of seconds) is below the threshold (~ 46 °C) of pain. These results strongly indicate that cutaneous perception of RF energy is not a reliable sensory response that will protect against potentially harmful levels of RF radiation over the broad frequency range of 0.5 MHz to 100 GHz.

5.7 OTHER PHYSIOLOGICAL AND BIOCHEMICAL EFFECTS

Charles G. Liddle

5.7.1 Clinical Chemistry and Metabolism

An individual's response to many stresses manifests itself through changes in some of the clinical chemistry indices. Serum calcium and phosphate levels normally increase initially and then decrease below normal in response to stress; whereas serum glucose, blood urea nitrogen, and uric acid levels increase following stress. These blood chemical responses are consistent with induction of release of adrenocortical hormones in response to stress. Physiological responses, including thermal responses, to RF-radiation exposure may occur at exposure levels too low to produce large changes in thermoregulatory behavior or colonic temperature. In such instances there may be changes in various metabolic parameters. There are few clinical chemistry and metabolism reports where exposures were sufficiently defined to relate results to the power density or SAR. These studies are described below, and are outlined in Table 5-19.

A study of the effects of microwaves on serum chemistry values was reported by Lovely _et_ _al_. (1977), who exposed rats in a circularly polarized waveguide to 918-MHz (CW) radiation. The animals were irradiated 10 h/day for 13 weeks at a power density of 2.5 mW/cm^2 (SAR ~ 1.04 W/kg). They reported no change in Na^+, K^+, ion gap, Cl^-, blood urea nitrogen, or glucose values compared to sham-irradiated animals. They did report a significant difference in the serum calcium values at the end of the 12-week exposure period.

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TABLE 5-19. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON CLINICAL CHEMISTRY AND METABOLISM, ENDOCRINOLOGY, AND GROWTH AND DEVELOPMENT

Effects	Species	Exposure Conditions					Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	Δt (°C)	
No effect on serum chemistry values	Rat	918 (CW)	2.5	91 x 600	1.0	0	Lovely et al. (1977)
Increase in serum glucose	Rabbit	2450 (CW and PW)	5, 10, 25	1 x 120	0.8-4.0 (est)	0, 0, 1.7 (PW) 0, 0, 2.9 (CW)	Wangemann and Cleary (1976)
Increase in blood urea nitrogen	Rabbit	2450 (CW)	25	1 x 120	4.0 (est)	2.9	
No increase in blood urea nitrogen	Rabbit Rabbit	2450 (CW) 2450 (PW)	5 and 10 5, 10, 25	1 x 120 1 x 120	0.8, 1.6 (est) 0.8-4.0 (est)	0 0, 0, 1.7	
Increased in uric acid values	Rabbit	2450 (CW and PW)	10, 25	1 x 120	1.6, 4.0 (est)	0, 1.7 (PW) 0, 2.9 (CW)	
			Neg^a 5		Neg 0.8	0	
No effect on other serum chemistry values	Rabbit	2450 (CW and PW)	5, 10, and 25	1 x 120	0.8-4.0 (est)	0, 0, 1.7 (PW) 0, 0, 2.9 (CW)	
Increased iron and manganese levels in brain	Rat	1600 (CW)	80	1 x 10	48 (est)	4.5	Chamness et al. (1976)
Decrease in specific metabolic rate (Ambient T = 24 °C)	Mouse	2450 (CW)	---	1 x 30	10.4 (Neg 5.5)		Ho and Edwards (1977b)
Increase in specific metabolic rate (Ambient T = 35 °C)	Mouse	2450 (CW)	---	1 x 30	8.6 (Neg 3.6)		Ho and Edwards (1979)
Increased NADH fluorescense Decreased ATP Decreased CP	Rat (exposed brain)	591 (CW)	13.8	1 x 0.5	0.36-2.2	0	Sanders et al. (1980)

(continued)

TABLE 5-19. (continued)

Effects	Species	Exposure Conditions Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	Δt (°C)	Reference
Decreased ATP Decreased CP	Rat (exposed brain)	591 (CW)	5	1 x 0.5	0.13-0.8	0	Sanders et al. (1980)
No effect on blood coagulation	Human plasma	2450 (CW)	10-280	1 x 30	1.3-38 (est)	Not reported	Boggs et al. (1972)
Increased thyroxine and tri-iodothyronine	Dog	2450 (CW)	72-236	1 x 120	58-190	Not reported	Magin et al. (1977a,b)
No effect on thyroid gland or thyroid hormone	Rat	2450 (CW)	1,10, 100 1, 10	1 x 10-45 56 x 480	0.25-25 0.25-2.5	≤ 10 mW/cm^2 = 0 100 mW/cm^2 ≥ 5	Milroy and Michaelson (1972)
No effect on thyroid function	Rat	2450 (CW)	10, 20, 25	1 x 240-960	2,5, 5, 6.25 (est)	≤ 20 mW/cm^2 = 0 25 mW/cm^2 = 1.7	Parker (1973)
Decrease in serum-protein-bound iodine, thyroxine and thyroxine/serum ratio	Rat	2450 (CW)	15	2.5 x 1440	3.8 (est)	0	Parker (1973)
Increase in thyroid hormone	Rabbit	3000 (PW)	5	48 x 180	0.25-0.75 (est)	Not reported	Baranski et al. (1972)
Decrease in serum thyroxine levels	Rat	2450 (CW)	20 Neg 1-10	1 x 240-480 1 x 60-480	5 0.25-25	0-0.6 0.6-1.4	Lu et al. (1977)
Increase in corticosterone levels	Rat	2450 (120 Hz AM)	40-70 Neg 1-20	1 x 60	8.4-14.7 Neg 0.21-4.2	1.3-3.0 0-0.6	Lu et al. (1981)
Decrease in thyrotropin levels			10, 40-70 Neg 1-5, 20		2.1-14.7 Neg 0.21-4.2	0-3.0 0-0.6	
Increase in corticosterone levels			10-40 Neg 1-5	1 x 240	2.1-8.4 Neg 0.2-1.0	0.3-2.1 0	
Decrease in thyrotropin levels			25, 40 Neg 1-20	5.2, 8.4 0.02-4.2	0.6-2.1 0-1		

(continued)

TABLE 5-19. (continued)

		Exposure Conditions					
Effects	Species	Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	Δt (°C)	Reference
No effect on thyroid, pituitary, or adrenal gland weight or growth hormone levels	Rat	2450 (CW)	1-20	1 x 60-480	0.25-25	0-1.4	Lu et al. (1977)
No effect on thyroid, anterior pituitary gland, adrenal, prostate or testes weights; no change in follicle stimulating hormone or gonadotropic hormone levels	Rat	2860-2880 (CW)	10	36 x 360	1-2 (est)	Not reported	Mikolajczyk (1976)
Increase in leutinizing hormone	Rat	2860-2880 (CW)	10	36 x 360	1-2 (est)	Not reported	Mikolajczyk (1976)
Increased adrenal weights and significant adrenal responses	Infant rat	2450 (CW)	40	6 x 5	20-60 (est)	1.5-2.5	Guillet and Michaelson (1977)
Increased plasma corticosterone levels	Rat	2450 (CW)	50, 60 Neg 13-40 20-40 Neg 13	1 x 30-60 1 x 120	11.5-13.8 (est) Neg 3.0-9.2 (est) 4.6-9.2 (est) Neg 13	13 mW/cm^2 = 0.5 20 mW/cm^2 = 0.7 30 mW/cm^2 = 0.9-1.4 40 mW/cm^2 = 1.3-1.4 50 mW/cm^2 = 1.6-2.4 60 mW/cm^2 = 2.5-2.9	Lotz and Michaelson (1978)
No effect on serum corticosterone levels	Rat	918 (CW)	2.5	91 x 600	1.0	0	Lovely et al. (1977)
No effect on weight gain	Rat	2450 (CW)	5	55 x 240	0.7-4.7	Not reported	Smialowicz et al. (1979a)

(continued)

TABLE 5-19. (continued)

Effects	Species	Exposure Conditions				Δt (°C)	Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)		
No effect on growth, neurological or immumological development or mutagenicity	Rat	100 MHz (CW)	46	112 x 240	2.8	Not reported	Smialowicz et al. (1981a)
Possible decrease in brain acetylcholinesterase activity				37, 55 x 240			
No effect on growth	Mouse	2450 (CW)	10	24 x 48	6-8 (est)	Not reported	McAfee et al. (1973)
No effect on body weights	Infant rat	2450 (CW)	40	6 x 5	20-60 (est)	1.5-2.5	Guillet and Michaelson (1977)
No effect on growth	Mouse	10.5, 19.27, 26.6 (CW)	8900	1 x 20	0.9, 1.8, 3.6 (est)	Not reported	Stavinoha et al. (1975)
	Mouse	19	17,000-114,000	5 x 40	6.3 (est)		
No effect on weight gain	Mouse	148 (CW)	0.5	50 x 60	0.013	Not reported	Lin et al. (1979a)

*Neg = Effect not found at value indicated.

However, this is most probably a spurious result because the calcium levels in the sham-irradiated animals were decreased from previous values, while the levels in the irradiated animals remained unchanged from earlier values. These results, therefore, mean that 918-microwaves at 2.5 mW/cm^2 do not alter the measured clinical chemistry values. Colonic temperature measurements were made on the animals, and no detectable changes were observed.

Somewhat differing from these results, Wangemann and Cleary (1976) reported an increase in serum glucose levels in rabbits exposed for 2 h to 2450-MHz microwaves (CW and PW) at power densities of 5, 10 and 25 mW/cm^2 (SAR's estimated at 0.8, 1.6, and 4.0 W/kg, respectively), and an increased blood urea nitrogen value in animals exposed to 25-mW/cm^2 microwaves only. Increased uric acid levels were found at 10 and 25 mW/cm^2 but not at 5 mW/cm^2 (both CW and PW). Levels of calcium, phosphorus, cholesterol, total protein, alkaline phosphatase, lactic dehydrogenase, and serum glutamic oxalic transaminase were unaffected at the three power densities. The authors stated that the PW and CW results could not be compared directly because the exposure conditions were different. The results were those that would be expected from heat stress. Animals exposed at 25 mW/cm^2 for 2 h showed a significant rectal temperature increase of 1.7 and 2.9 °C for PW and CW exposures, respectively. Those exposed at 10 mW/cm^2 showed evidence of mild heat stress, such as peripheral vasodilation, but no significant increase in rectal temperature. One possible explanation for the difference between these results and those of Lovely _et al_. is the difference in absorbed energy patterns in rats and rabbits at 2450 MHz.

Brains from rats exposed at 1600 MHz for 10 min at a power density of 80 mW/cm^2 (SAR estimated at 48 W/kg) were analyzed for selected heavy metals by Chamness et al. (1976). Iron levels were increased in all the areas of the brain (hypothalamus, corpus striatum, midbrain, hippocampus, cerebellum, medulla, cortex). Manganese was increased in the cortex and medulla, and copper was increased in the cortex; while calcium, zinc, sodium, and potassium levels were unchanged. The observed changes were probably a result of hyperthermia since most alterations seen were also observed in rats subjected to a hyperthermal environment, and the irradiated animals showed a rectal temperature increase of 4.5 °C.

Platelet-rich human plasma was irradiated in vitro with 2450-MHz microwaves at power densities of 10 to 280 mW/cm^2 (SAR's of 1.3 to 38 W/kg) for 0.5 to 24 h by Boggs et al. (1972), and effects on blood coagulation were analyzed. They reported no significant changes in platelet count, coagulation time, or clot strength at these power densities. The plasma temperature was maintained below 37 °C during the exposures. They also conducted studies on the effect of heating on coagulation time and clot strength. Samples were heated either by microwaves or by radiant heating, and the results were compared to unheated control samples. The relative coagulation time for the microwave-heated samples remained unchanged throughout the temperature range studied (34, 37, 39 and 42 °C), while the samples heated by radiant energy showed increases in the relative coagulation time (1.58 and 2.03 times the non-heated samples) at 39 and 42°C, respectively. A similar, but reverse effect was seen in the relative clot strength. The samples heated to 42 °C by microwaves showed a decrease to 0.74 times the control samples, while the radiant-heated samples showed a decrease to 0.31 times the control values. A possible explanation for these differences is the difficulty of producing the same heating rate and pattern within a sample using different sources of heat.

Ho and Edwards (1977b) measured the rate of oxygen consumption of mice exposed to 2450-MHz microwaves in a waveguide for 30 min at dose rates from 1.6 to 44.3 W/kg at an environmental temperature of 24 °C. They found a significant decrease in the specific metabolic rate (SMR) at 10.4 W/kg or higher, but not at 1.5 or 5.5 W/kg. There was no detectable rectal temperature increase at or below 10.4 W/kg, but there was a 0.5 °C increase at 23.6 W/kg and a 1.0 °C increase at 44.3 W/kg. These results indicate that the mouse compensates for large dose rates of microwave energy by adjusting its metabolic rate downward to compensate for the thermal load.

In a more recent report, Ho and Edwards (1979) reported a continuation of the previous study. Exposure conditions were identical to those of the previous study except that environmental temperatures of 20, 30, and 35 °C were also used. At 20 °C they found a significant decrease during exposure in the SMR at 12.1 W/kg and above, but not at 6.0 W/kg or below. A significant decrease was found in the SMR during the 30-min post-exposure period at 45.1 W/kg, but not at 27.0 W/kg or less. For the exposures at 30 °C there was no change in the SMR at any of the dose rates used (1.4 to 23.7 W/kg) either during exposure or in the post-exposure period. At 35 °C there was a significant increase in the SMR at 8.6 W/kg and higher, but not at 3.6 W/kg or lower during exposure, and no changes were observed during the postexposure period. The authors re-evaluated their first report (Ho and Edwards 1977b) by comparing the results during exposure to the pre-exposure values instead of comparing the values of the animals during exposure with those of sham-exposed animals. With this method of evaluation, the SMR values during exposure at 24 °C were not significantly different from the pre-exposure values. They reported that this method of comparison accounted for the lack of uniformity among animals at the beginning of each experiment and therefore was a better method of comparison.

The general trends indicated by their studies are that microwave exposure at the lowest ambient temperature resulted in a reduction in the SMR, exposure at the highest ambient temperature resulted in an increase in the SMR, and no significant changes occurred at the intermediate temperatures. A possible interpretation of these trends is that at the lower ambient temperatures the animals are producing heat to maintain thermal neutrality; addition of the microwave heating reduces the animals' demand for additional heat. At the higher amibent temperatures the animals may be actively trying to dissipate the additional heat from the microwaves, thereby increasing their SMR.

A study on the effects of microwaves on energy metabolism of the rat brain was reported by Sanders _et al_. (1980). First, a small area of the brain of anesthetized animals was surgically exposed. Then a horn antenna was positioned so that exposures were in the far field and only the exposed surface of the brain was irradiated with the electric field parallel to the body axis. Animals were exposed to 591-MHz (CW) radiation for 0.5, 1, 2, 3, or 5 min at 13.8 mW/cm^2 or for 0.5 or 1 min at 5 mW/cm^2. (Calculated SAR for

5 mW/cm^2 = 0.13 W/kg using a 2-cm sphere model or 0.8 W/kg using a semi-infinite plane model.) During exposures at 13.8 mW/cm^2 they found an increase in nicotinamide adenine dinucleotide (NADH) fluorescence to a maximum of 4.0 to 12.5 percent above pre-exposure control levels. In addition, adenosine triphosphate (ATP) levels were significantly decreased at all exposure times, as were creatine phosphate (CP) levels. At 5 mW/cm^2, ATP and CP levels were also significantly decreased following 0.5- and 1-min exposures. The ATP and CP changes at 5 mW/cm^2 were not significantly different from those seen at 13.8 mW/cm^2. There were no changes in rectal temperature at any of the exposures and no significant difference in brain temperature between exposed and sham-exposed animals. The authors concluded that the results (increased NADH fluorescence; decreased ATP and CP levels) support the hypothesis that RF radiation inhibits mitochondrial electron transport chain function and that the changes cannot be attributed to general tissue hyperthermia.

In summary, changes in clinical chemistry values have been reported at dose rates as low as 0.8 W/kg in rabbits, and negative results have been reported at exposures as high as 1 W/kg in rats. The clincial chemistry changes that have been reported are those that would be expected from heat stress. In other studies, effects on the rate of oxygen consumption of mice have been reported at 9.6 W/kg but not at 5.5 W/kg, and changes in brain energy metabolism have been found at 0.13 to 0.8 W/kg (Table 5-19).

5.7.2 Endocrinology

The endocrine system in coordination with the nervous system is a major regulatory system in the body. Alterations in the function of the neuroendocrine system often reflect the efforts on the part of the animal to maintain homeostasis when subjected to stressful internal and external stimuli. Detection of changes in the endocrine system is a sensitive means of analyzing the animal's responses either to direct stimulation of the endocrine organs themselves or to stimulation of the CNS. The thyroid gland plays a basic role in regulating basal metabolism as well as in generating metabolic heat in the tissues. Changes in thyroid activity can result from changes in thyroid-stimulating hormone from the hypothalamic-hypophyseal system and/or increased metabolic activity of the thyroid gland due to heating. Direct interaction with the CNS could also produce changes in thyroid activity. Moderate or gradual heating results in a reduction of thyroid hormone, while rapid or marked elevation of body temperature results in an increase in thyroid activity. The results of RF-radiation-effects studies on the endocrine system are discussed below and summarized in Table 5-19.

Thyroid function of rats following exposure to 2.45-GHz microwaves at 10, 20, and 25 mW/cm^2 (SAR's estimated at 0.25 W/kg per mW/cm^2) for 4 or 16 h was studied by Parker (1973). No effects on thyroid gland function were found at these exposures. However, at 15 mW/cm^2 (SAR estimated at 3.75 W/kg), exposure for a longer period (60 h) was reported to produce a significant decrease in serum-protein-bound iodine, thyroxine and thyroid/serum iodine ratio. A significant rectal temperature increase (1.7 °C) was reported at 25 mW/cm^2, but not at lower power densities.

Magin et al. (1977a, b) irradiated the surgically exposed thyroid gland of anesthetized dogs with 2450-MHz (CW) microwaves using a waveguide applicator at power densities from 72, 162, and 236 mW/cm^2 (SAR's from 58 to 190 W/kg) for 2 h. One thyroid was irradiated while the other was used as a control. Tissue temperatures of 39, 41, and 45 °C were maintained in the thyroid at the three power densities. They reported an increased release of thyroxine (TH) and triiodothyronine (T3) at all power densities, demonstrating that the thyroid gland in the dog can be stimulated directly by microwave heating.

Milroy and Michaelson (1972), who exposed rats to 2450-MHz microwaves at 1, 10, and 100 mW/cm^2 (SAR = 0.25 W/kg per mW/cm^2) for single exposures of 10, 20, 30, and 45 min and at 1 and 10 mW/cm^2 8 h/day for 8 weeks, reported no effect on T3 levels, thyroxine levels, or on the uptake of radioactive iodine. No rectal temperature increase was observed at 10 mW/cm^2 or less. At 100 mW/cm^2 there was a constant rise in rectal temperature throughout exposure, up to 42 °C at the end of the exposure period. Histopathological examination of the thyroid glands also showed no effect from the exposure.

An increased production of thyroid hormone in rabbits as measured by increased incorporation of ^{131}I and increased radioactivity per gram of thyroid (verified by autoradiography) was reported by Baranski et al. (1972). The animals were exposed for 3 h/day for 4 months to 10-cm (3-GHz, PW) microwaves at an average incident power density of 5 mW/cm^2 (SAR estimated at 0.25 to 0.75 W/kg). They reported no increase in body temperature or thyroid temperature. (The pulse parameters were not given, so peak power density cannot be calculated.)

Lu _et_ _al_. (1977) reported serum thyroxine levels in rats exposed to 2450-MHz microwaves at 1, 5, 10, and 20 mW/cm^2 (0.25, 1.25, 2.5, and 5 W/kg) for 1, 2, 4, or 8 h. Decreased thyroxine levels were observed at 20 mW/cm^2 following 4- and 8-h exposures. The thyroxine values at shorter exposures and lower power densities were not significantly different from the sham values, except for an increase after 4 h at 1 mW/cm^2, which appears to be a chance variation, since at both higher and lower power densities and at longer and shorter periods of exposure no effect was detected. There were small but statistically significant rectal temperature increases at 1 mW/cm^2 after 4 h, at 5 mW/cm^2 after 1 and 2 h, and at 10 mW/cm^2 after 2 and 4 h of exposure. The increases were in the 0.2 to 0.56 °C range. The lack of correlation between power density, exposure time, and rectal temperature increase, along with the small rectal temperature change, suggests that the effects may not have been due entirely to the microwave exposure but possibly from the stress of confinement. At 20 mW/cm^2, however, the rectal temperature was significantly elevated at all four exposure times and tended to increase with longer exposures. At 1 and 2 h the changes were small (0.64 and 0.54 °C), but larger (1.01 and 1.35 °C) increases occurred after 4 and 8 h. Serum corticosteroid levels were decreased at 20 mW/cm^2 after 8 h only, which the authors report as a shift in the circadian periodicity. Serum growth hormone measurements showed no change at any of the power densities or times reported. They also measured no change in the mass of the thyroid, pituitary, and adrenal glands following irradiation.

In another study on the effects of microwaves on acute endocrine responses in rats, Lu _et_ _al_. (1981) exposed animals to 2.45-GHz microwaves (AM at 120 Hz) for 1 and 4 h, and measured colonic temperature, thyrotropin, and corticosterone levels immediately after exposure. The 1-h exposures were conducted at power densities of 1, 5, 10, 20, 40, 50, 60, or 70 mW/cm^2, and the 4-h exposures at 0.1, 1, 5, 10, 20, 25, and 40 mW/cm^2 (measured SAR = 0.21 W/kg per mW/cm^2). The results for the 1-h exposure showed an increase in colonic temperature with increasing power density with a significant increase at 20 mW/cm^2 and above, but not at 10 mW/cm^2 or below. Corticosterone also showed an increase with increased power density with evidence of a threshold between 20 and 40 mW/cm^2. Thyrotropin values showed a decrease with increasing power densities, significant results at 40 mW/cm^2 and above, and equivocal results in the 10 to 20 mW/cm^2 range (10 mW/cm^2 values were significantly lower while those at 20 mW/cm^2 were not). Similar trends were observed following 4-h exposures, with a significant increase in colonic temperatures at 10 mW/cm^2 and above, and no increases at 5 mW/cm^2 or below with the exception of one small group at 1 mW/cm^2. The trends for the increase in corticosterone levels and the decrease in thyrotropin levels were not significant; however, the corticosterone level at 40 mW/cm^2 was significantly increased, but not at 25 mW/cm^2 or lower values. Also, the thyrotropin values at 25 mW/cm^2 and 40 mW/cm^2 were significantly decreased, whereas those at 20 mW/cm^2 and below were not. Comparing the effects of 1- and 4-h exposures on the three parameters, the change in colonic temperature was similar for both exposures; however, the stimulatory effect on serum corticosterone levels was less for the 4-h exposures than for the 1-h exposures, while the depression of serum thyrotropin was more pronounced after 4 h than after 1 h. The authors concluded that the hormonal changes probably represented a general nonspecific stress reaction that was related to the intensity and duration of the stressing agent, rather than to the nature of the agent itself.

No change in thyroid weight was seen in a study by Mikolajczyk (1976), where rats were exposed to 2860 to 2880-MHz microwaves at 10 mW/cm^2, 6 h/day, 6 days/week for 6 weeks. The SAR is estimated to be 1 to 2 W/kg for a single animal exposure, but the animals were exposed close together in a box with dividers every 10 cm, which should give a somewhat higher SAR value. The author did find a significant increase in luteinizing hormone from the anterior pituitary gland but no change in follicle-stimulating or gonadotropic hormone levels. The weights of the anterior pituitary, adrenal, prostate, or testes were not affected by the exposure.

Other investigators also have reported the effects of microwaves on adrenal function. An increase in blood-corticosteroid concentration above that which would normally occur at that time of day in the absence of a stimulus is considered by many to be an indicator of an animal's response to stress. This results when an internal or external stimulus, either chemical, physical, or emotional, excites neurons of the hypothalamus to release corticotropin-releasing hormone, which drives the pituitary to release adrenocorticotropic hormone (ACTH). This hormone then stimulates the adrenal cortex to secrete corticosteroids. Among the strongest stressful stimuli are surgery, anesthesia, cold, narcosis, burning, high environmental temperature, and rough handling or restraint. Additional studies examining the effects of microwaves on adrenal function are described below.

Lovely et al. (1977) exposed rats to 918-MHz microwaves at 2.5 mW/cm^2 (SAR ~ 1.04 W/kg), 10 h/day for 13 weeks, and observed no changes in serum corticosterone levels. In a study by Guillet and Michaelson (1977), rat pups were exposed to 2450-MHz microwaves at 40 mW/cm^2 (SAR estimated at 20 to 60 W/kg), 5 min/day for 6 days beginning at day 1 postpartum; no change in basal corticosterone levels was found. There was a significant adrenal response to the microwaves, but this was the same as seen following ACTH administration, indicating a stress reaction. Rectal temperatures of the exposed animals averaged 1.5 to 2.5 °C higher than those of the sham-exposed animals. Adrenal mass of the irradiated animals was significantly greater than those of the control animals.

In another study, Lotz and Michaelson (1978) irradiated rats with 2450-MHz microwaves at power densities of 13, 20, 30, and 40 mW/cm^2 for 30, 60, or 120 min and at 50 and 60 mW/cm^2 for 30 or 60 min (SAR estimated at 0.21 W/kg per mW/cm^2). Plasma corticosterone levels were increased at power densities at or above 50 mW/cm^2, but not at 40 mW/cm^2 or less, for the 30- and 60-min exposures. At the longest exposure time (120 min), increased levels were seen at or above 20 mW/cm^2 but not at 13 mW/cm^2. Graphs were presented of the rectal temperatures taken at the completion of exposures; estimates of the rectal temperature increases taken from the graphs for 50 mW/cm^2 were 1.6 and 2.4 °C and for 60 mW/cm^2 were 2.5 and 2.9 °C for 30 and 60 min, respectively. The temperature increases for 40 mW/cm^2 were 1.3 and 1.4 °C for 30 and 60 min. For the 120-min exposures, rectal temperature increased 0.5 °C at 13 mW/cm^2 and 0.7 °C at 20 mW/cm^2.

In summary, microwave effects on thyroid function have been reported at SAR's as low as 2.1 W/kg, and negative results have been reported at values as high as 25 W/kg. The duration of exposure as well as the exposure rate appears to be important, as demonstrated by the study of Parker (1973), where exposures at 6.25 W/kg for 16 h produced no changes, while 3.75-W/kg exposures for 60 h resulted in a decrease in serum thyroxine levels. Changes in corticosterone levels have been reported from microwave exposure at SAR's as low as 10 W/kg but not at 6.25 W/kg, and adrenal responses have been reported at levels as low as 4.6 W/kg but not at 3 W/kg.

5.7.3 Growth and Development

Few investigators have reported the effects of a combination of pre- and postnatal exposure or postnatal exposure only to RF radiation on the growth of laboratory animals. Smialowicz _et_ _al_. (1979a) exposed rats for 4 h per day, beginning on day 6 of gestation through 40 to 41 days postpartum to 2450-MHz (CW) microwaves at 5 mW/cm^2 (SAR's = 0.7 to 4.7 W/kg), and reported no difference between the weight gains of the exposed and sham-exposed animals.

In another study, Smialowicz _et_ _al_. (1981a) reported the growth and development of rats exposed to 100-MHz (CW) microwaves at an incident power density of 46 mW/cm^2 (average SAR = 2.8 W/kg) for 4 h/day from day 6 of gestation through 97 days of age. There was no consistent difference between the body weights of the exposed and sham-exposed animals, though the exposed animals tended to be larger than the sham-exposed animals. Some of the animals were tested for neurological development, and no differences were observed in the development of a startle response or righting reflex. There was a significant difference in the age of eye opening, with the mean age of eye opening in the sham-irradiated animals occurring almost one day later than the irradiated animals. The authors stated that the change probably did not represent an acceleration of eye opening, as the age of eye opening in the irradiated animals was similar to that normally seen in control animals in other experiments, but also mentioned that eye opening was delayed in the sham-irradiated animals. Tests for development of motor activity at 35 and 84 days of age showed no difference between exposed and sham-exposed animals. No difference was observed for complete blood counts, mitogen-stimulated response of lymphocytes, frequency of T- and B-lymphocytes, or antibody response to Streptococcus pneumoniae capsular polysaccharide between the exposed and sham-exposed animals. No mutagenic effect was observed on the sperm cells after 20 days using the dominant lethal assay. Seven regions of the brain were weighed at 22, 40, and 97 days of age, and there was a significant increase in the weight of the medulla in the irradiated animals at 40 days of age but not at 22 or 97 days of age. There were no differences in the weights of any other brain region. There were also no differences in the brain protein concentrations for the seven regions. Brain acetylcholinesterase (AChE) activity, however, was reduced in the striatum and medulla at 22 days of age and in the midbrain at 40 days of age. No effects on AChE activity were noted in the other regions at 22 and 40 days of age, and no differences were noted at 97 days of age. The differences were small, and there appeared to be no pattern to the changes; the sample size was small (3 to 5 animals), and out of 21 comparisons made at the 5 percent confidence level, one significantly different result would be expected. Consequently, without replication with a larger sample size, it is difficult to ascribe these changes to the microwave exposure.

The effect of postnatal exposure to microwaves on growth and development was studied by McAfee et al. (1973). Weanling mice were exposed to 2450-MHz microwaves at 10 mW/cm^2, 2 min each hour for 24 days; no effect on animal growth was found. There was no elevation of body temperature in the exposed animals. The authors also stated that a previous study, in which a stimulatory effect on growth from microwaves was claimed, was probably in error because of inaccuracies in weighing the animals (see Nieset et al. 1958).

Guillet and Michaelson (1977) exposed neonatal rats to 2450-MHz microwaves at 40 mW/cm^2 (SAR's at 20 to 60 W/kg), 5 min/day for 6 days beginning on day 1 postpartum. No effect on body mass was found, though the authors did report adrenal changes, as discussed in the previous section, § 5.7.2, Endocrinology.

Stavinoha et al. (1975) irradiated 4-day-old mice at a field intensity of 5800 V/m (8.92 W/cm^2) for 20 min with 10.5-, 19.27-, or 26.6-MHz radiation, and observed no change in growth rate to 22 days of age compared to the control animals (SAR's estimated at 0.9, 1.8, and 3.6 W/kg). Mice were also exposed to 19-MHz microwaves for 40 min/day for 5 days using a near-field synthesizer to deliver an E field of 800 V/m (17 W/cm^2) and an H field of 55 A/m (114 W/cm^2); no change in body mass through 120 days of age was found (SAR estimated at 6.3 W/kg).

In a chronic study, Lin et al. (1979a) exposed 4- to 7-day-old mice to 148-MHz microwaves at 0.5 mW/cm^2 (SAR = 0.013 W/kg), 1 h/day, 5 days/week for 10 weeks and reported no significant effect on weight gain.

These studies indicate that RF exposures at SAR's $\leq$ 8 W/kg have no effect on growth and development of animals exposed pre- and postnatally or postnatally only. Exposures at 20 to 60 W/kg postnatally for short exposure times also did not alter the growth rate of animals even though adrenal changes were seen.

5.7.4 Cardiovascular System

5.7.4.1 Whole-Body Exposures--

Some of the initial studies of biological effects of microwave radiation were made on the cardiovascular system. Presman and Levitina (1962) reported that whole-body or ventral exposure to CW microwaves at 2400 MHz, 7 to 12 mW/cm^2, promoted a decreased heart rate (bradycardia) in the rabbit. However, exposing only the head to microwaves at the same power densities resulted in an increased heart rate (tachycardia).

Kaplan et al. (1971) attempted to replicate the tachycardia reported by Presman and Levitina by exposing the head of rabbits to 2400-MHz (CW) microwaves at an incident power density of 10 mW/cm^2 (SAR estimated at 2 W/kg). The exposure conditions differed in that Kaplan et al. exposed the animals in the far field, while Presman and Levitina used near-field exposures. Kaplan et al. reported no change in heart rate. They then exposed rabbits at increasing power densities (20, 40, 60, 80, and 100 mW/cm^2) and measured respiration rate, body temperature, and heart rate. Respiration increased at 40 mW/cm^2 and greater, and body temperature was elevated at 80 and 100 mW/cm^2 (0.5 °C at both power densities). Heart rate increased at 100 mW/cm^2 only.

Birenbaum et al. (1975) exposed the heads of unanesthetized rabbits to 2.4-GHz (CW) microwaves for 60 min at 20, 40, 60, and 80 mW/cm^2 (SAR estimated at 3 to 12 W/kg), and found increases in heart rate, respiration rate, and subcutaneous temperature (lower back) at all four power densities, with greater increases at higher exposure levels. They also compared 2.8-GHz (CW and PW, 1000/s, 1.3 μs) microwaves at 20 mW/cm^2 for the same three parameters and found no differences in the responses to CW or PW irradiation.

Phillips et al. (1975b) exposed adult rats to 2450-MHz microwaves pulsed at 120 Hz for 30 min (SAR's = 4.5, 6.5, and 11.1 W/kg) and measured colonic and skin temperatures and heart rate after exposure. They reported increases in colonic and skin temperatures with increased exposure levels immediately after irradiation. At the highest exposure, the colonic temperature dropped below normal at 1 h after exposure and remained subnormal for 4 h. There was no post-exposure effect on heart rate at 4.5 W/kg; however, there was a mild bradycardia at 6.5 W/kg and a more pronounced decrease in heart rate at 11.1 W/kg. They attributed the effect to the heat stress induced by the microwaves.

Hamrick and McRee (1980) assessed the effects of body temperature on the heart rate of embryonic quail. They exposed the embryos to 2450-MHz (CW) microwaves for 5 to 10 min (SAR's = 3, 6, 15, and 30 W/kg) at incubation temperatures from 35 to 38 °C, and to 2450-MHz (PW) microwaves (10-μs pulses, varied from 10 to 50 pulses/s, SAR's at 0.3, 1.5, and 3 W/kg) at incubation temperatures of 35 to 39 °C. There were no significant differences between the heart rates of the exposed and control embryos in any of the groups at any of the temperatures used. They did observe that the embryonic heart rate increased ~ 23 beats/min for each °C rise in incubation temperature in the 36 to 39 °C range.

5.7.4.2 Isolated Heart Preparations--

Although the data supporting a microwave-induced bradycardia in the intact animal are equivocal, some researchers have exposed isolated heart preparations and reported an effect of microwaves on heart rate. Tinney _et al_. (1976) attempted to determine the locus of microwave-induced bradycardia in the isolated turtle heart using 960-MHz (CW) microwaves. Although the heart was isolated from the CNS, it was still capable of responding to neurohumoral agents. They found that exposing the isolated heart to microwaves at 8 mW/cm^2 caused bradycardia. When the heart was treated with atropine, blocking the sympathetic system, tachycardia resulted. However, when the heart was treated with propranolol, blocking the parasympathetic system, the heart rate decrease was more significant than that following microwave exposure alone, indicating that microwaves may have affected the parasympathetic reflexes. With both blocking agents added to the heart, microwave exposure had only slight effects on the heart rate. Tinney _et al_. postulated that microwave exposure of the isolated heart equally enhances the release of acetylcholine and norepinephrine; however, since the activity of the former usually predominates over the latter (Johansen 1963), the net effect of microwave exposure is a decrease in heart rate.

A similar drug-microwave interaction has been observed in the isolated rat heart by Olsen _et_ _al_. (1977). They exposed the heart to 960-MHz (CW) microwaves for 4 min at 1.3 and 2.1 W/kg and observed a decrease in heart rate. The decrease was greater at 1.3 W/kg than at 2.1 W/kg. They also conducted studies at 2.1 W/kg with drugs to block the sympathetic and parasympathetic nervous system and obtained the same results as Tinney _et_ _al_. (1976).

Paff _et_ _al_. (1963), working with the isolated embryonic chicken heart, were unable to detect changes in heart rate during exposure to 24,000-MHz fields. They did, however, detect effects on the electrocardiogram (ECG), including abnormal P and T waves from 3-min exposures at 74 mW/cm^2.

Frey and Seifert (1968) showed that 10-μs pulses at a carrier frequency of 1.425 GHz given at a synchronous period with the ECG (220 ms after the P wave) resulted in tachycardia or heart arrhythmia in the isolated frog heart. The peak power density was 60 mW/cm^2 (average power density ~ 0.6 $\mu W/cm^2$). Liu _et_ _al_. (1976) reported no effect on heart rate with isolated frog hearts or in hearts irradiated _in_ _situ_ in a similar study. The _in_ _situ_ hearts were exposed to 100-μs pulses of either 1.42 or 10 GHz, and the isolated frog hearts were exposed to 100-μs pulses of 1.42 GHz. The pulse was delivered on the rising phase of the R-wave from the ECG, which was somewhat similar to, but not exactly the same as, the 200-ms delay following the P-wave used by Frey and Seifert. (The R-wave follows the P-wave by around 200 ms.) The peak and average power densities of 320 mW and 32 μW were also considerably higher than those used by Frey and Seifert. These factors, plus differences in the manner of preparing the isolated hearts (Liu et al. curarized the frogs, whereas Frey and Seifert decapitated the frogs), make it difficult to compare the results of the two studies.

Clapman and Cain (1975), however, tried to replicate the study of Frey and Seifert using similar pulse widths (10 μs), peak and average power densities (60 mW/cm^2 and 0.6 $\mu W/cm^2$), carrier frequency (1.42 GHz), and method of isolating the frog heart; they reported no change in heart rate. When they conducted studies with a different peak power (5.5 W/cm^2), frequency (3 GHz), and pulse widths (2 and 150 μs), they also found no heart rate changes. Clapman and Cain were able to produce an increased heart rate with 20-mA current pulses synchronized 200 ms after the P-wave peak.

The results of microwave exposure on the cardiovascular system indicate that whole-body exposures of sufficient intensity to produce heating will also produce an increase in heart rate similar to that which would be expected from heating alone. In the isolated heart there appears to be a stimulation of the autonomic nervous system from microwave exposure at levels where little heating would be expected (1 to 2 W/kg). Low levels of synchronized PW microwaves (0.6 to 32 mW/kg) apparently are ineffective in producing detectable alterations in heart rate. A summary of the RF-radiation effects on cardiac physiology is given in Table 5-20.

5.7.5 Calcium Ion Efflux

Calcium ions play a prominent role in many biochemical and biophysical processes. They are involved in maintaining cellular membrane integrity and function, as a cofactor in many enzyme reactions, as a putative second messenger for the conduction of extracellular signals to the nucleus of the cell, and in neural tissue for excitation and for the secretion of transmitter substances at synapses. Several investigators have reported the effects of electromagnetic fields on the response of calcium ions in biological systems, principally brain tissue. Bawin et al. (1975) showed that a 20-min in vitro exposure of chicken brain tissue to a 147-MHz field, at a power density of 1 to 2 mW/cm^2, could cause enhanced efflux of calcium ions from the samples, but only if the field was sinusoidally amplitude modulated with frequencies of 6, 9, 11, 16, or 20 Hz. Maximal efflux was measured at 16 Hz. Modulation frequencies of 0, 0.5, 3, 25, or 35 Hz were ineffective. This result was corroborated and extended by Blackman et al. (1979, 1980a), who showed that the response occurred only within a narrow intensity range around 0.83 mW/cm^2. Sheppard et al. (1979) confirmed this intensity response with a 450-MHz carrier wave amplitude modulated at 16 Hz; calcium efflux was enhanced at 0.1 and 1.0 mW/cm^2 but not at 0.05, 2.0, or 5.0 mW/cm^2.

Blackman and co-workers also examined the influence of 50-MHz fields, amplitude modulated at 16 Hz, and found that the response could be elicited

TABLE 5-20. SUMMARY OF STUDIES CONCERNING RF-RADIATION EFFECTS ON VARIOUS ASPECTS OF CARDIAC PHYSIOLOGY

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm^2)	Duration (total min)	SAR (W/kg)	
Bradycardia develops after whole-body exposure along with hyperthermia	Rat	2,450 (PW)	28 & 48	30	6.5 & 11.1	Phillips et al. (1975b)
Exposure to head promotes tachycardia, exposure to back raises respiratory rate but not heart rate	Rabbit	2,450 (CW and PW)	20	60	3	Birenbaum et al. (1975)
Increased respiration	Rabbit	2,400	40-100	20	8-20	Kaplan et al. (1971)
Increased heart rate from dorsal exposure of the head	Rabbit	2,400	100	20	20	Kaplan et al. (1971)
Alterations in ECG (shortening of QT interval, increased height of T-wave, appearance of U-wave)	72-h chick heart	24,000 (PW)	74	3	NG	Paff et al. (1963)
No effect on heart rate that cannot be attributed to microwave heating	Quail embryo	2,450 (CW and PW)	NA*	5 to 10	0.3-30	Hamrick and McRee (1980)
Pulses synchronized with each R-wave do not affect heart rate	Frog	1,420-10,000 (PW)	NA	100-μs pulses	12 or 16 μW per heart	Liu et al. (1976)
Synchronized pulses with QRS complex causes increase in heart rate with some arrhythmias	Frog	1,425 (PW)	0.6 μW/cm^2	10-μs pulses	NG	Frey and Seifert (1968)

(continued)

TABLE 5-20 (continued)

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm^2)	Duration (total min)	SAR (W/kg)	
Low power levels cause bradycardia in the isolated turtle heart	Turtle	960 (CW)	NA	60	2-10	Tinney et al. (1976)
Causes slight decrease in the isolated heart	Rat	960 (CW)	NA	5 to 10	1.3 and 2.1	Olsen et al. (1977)
Synchronized exposures with ECG have no effect on heart rate	Frog	1420-3000 (PW)	0.0006	2-, 10-, 150-μs pulses	NG	Clapman and Cain (1975)

*NA = Not applicable.

within two intensity regions (between 1.44 and 1.67, and at 3.64 mW/cm^2) separated by power densities of no effect including 0.72 mW/cm^2 (Blackman et al. 1980b). The apparent discrepancy in the calcium ion efflux data at different power densities at the three different carrier frequencies (50, 147, and 450 MHz) has been resolved by the finding that the efflux is dependent upon the electric field strength within the sample and not on the incident power density (Joines and Blackman 1980). The empirical model used to transform the incident power density to internal field strength has also been used to predict additional values of intensity that produced both alteration and no alteration in calcium ion efflux (Joines and Blackman 1980). It should be noted that the 147-MHz and 50-MHz exposures caused no generalized heating of the sample. The maximum temperature rise was calculated to be less than 0.0004 °C, and calculated SAR's at each carrier frequency were less than 0.0014 W/kg (Blackman et al. 1980b).

Although outside the range of the frequencies of interest for this review, frequencies within the same 6- to 20-Hz region applied directly, without a carrier wave, were demonstrated to alter the efflux of calcium ions from chicken brain tissue (Bawin and Adey 1976). In this case, the efflux of calcium ions was reduced by the exposure. At the intensities used, there is no heating of the sample exposed to 6- to 20-Hz fields because energy absorption is very small.

No change in calcium ion efflux from brain tissue has been reported by Shelton and Merritt (1981), who used procedures somewhat different from those described by Bawin et al. (1975), Bawin and Adey (1976), and Blackman et al.

(1979, 1980a). They irradiated brain tissue from the rat with 1-GHz radiation, square-wave, pulse-modulated at 16 Hz (0.5, 1.0, 2.0, or 15 mW/cm^2). In their original study, Bawin et al. (1975) also exposed skeletal muscle to the same exposure conditions that produced calcium ion efflux from chick brain tissue, but no effect was observed.

An increase of calcium ion efflux from rat pancreatic tissue exposed at 2 mW/cm^2 for 1 to 2.5 h at 147 MHz, sinusoidally amplitude modulated at 16 Hz (estimated SAR < 0.075 W/kg), has been reported by Albert et al. (1980). However, the efflux was not accompanied by a change in protein secretion, which is normally associated with calcium mobilization in the pancreas. The authors attributed the lack of protein secretion to the relatively small volume of medium available to the tissue slices for normal metabolic activity.

Although the efflux of calcium ion from chick brain tissue has been documented in two laboratories, the mechanism of the effect and physiological significance are still highly uncertain. These points are addressed in more detail in Unresolved Questions.

5.7.6 Unresolved Questions

No report has yet described a mechanism of action in sufficient detail to identify all the relevant conditions necessary and sufficient to unequivocally explain the calcium ion response in the brain or pancreas. The response to specific intensities is unusual and presently unexplained. Any critical evaluation of this phenomenon, particularly in brain tissue, must also consider corollary supporting studies with brain tissue from cats (Bawin and Adey 1977), cat brain tissue *in vivo* (Kaczmarek and Adey 1973), and specific brain rhythms in cats (Bawin *et al*. 1973), as well as behavioral changes in monkeys (Gavalas-Medici and Day-Magdaleno 1976). This response to modulation of an RF-carrier wave or to sub-ELF signals alone may be a true field effect at a very low SAR and at biologically relevant frequencies, i.e., in the range of frequencies normally present in the electroencephalogram (EEG).

Other areas where there are unanswered questions is in comparisons of CW vs. PW microwaves under identical exposure conditions. Such studies would help determine if the differences seen by Wangemann and Cleary (1976) were due to different exposure conditions or to the irradiation parameters (CW or PW).

There is also a paucity of information on the effects of RF radiation at different frequencies, particularly at frequencies of environmental importance. Studies at different frequencies would help to determine the reasons for differences in effects at similar SAR's. Such studies might help explain why Wangemann and Cleary (1976) reported serum chemistry changes in rabbits at 0.8 W/kg (2450 MHz), and why Lovely *et al*. (1977) reported no change in serum chemistry values in rats at 1 W/kg (918 MHz).

There are also data such as those by Boggs *et al*. (1972) where the results from microwave heating to a predetermined temperature are different from those resulting from the same temperature produced by other means of heating. Perhaps there are differences in the uniformity of heating or the rate of heating that would account for these differences. Additionally, a study by Deficis et al. (1979) reported elevated serum triglyceride and β-lipoprotein levels in mice exposed to 2450-MHz microwaves at power densities of 1.5, 3.3, and 4 mW/cm^2, but not at 1 mW/cm^2. Because the exposures were conducted in a multimodal cavity, SAR values were not reported and cannot be predicted. If this study is repeated, particular attention should be given to dosimetry. An alternative is to make or report dosimetric measurements in the exposure system used.

The reported effects of thyroid function at 3.75 W/kg for 60 h contrasted with no effect at 6.25 W/kg for 16 h (Parker 1973) suggests that the total amount of energy absorbed may also be an important consideration. Additional studies could define further the relative importance of dose rate compared with total dose.

5.8 GENETICS AND MUTAGENESIS

Carl F. Blackman

5.8.1 Introduction

Genetics is the branch of biology that deals with the heredity and variation of organisms. The biochemical basis of heredity lies in the sequence of bases found in the nucleic acids, deoxyribonucleic acid (DNA), and in a few cases, ribonucleic acid (RNA). All living cells have the biochemical machinery to detect the sequence of bases in the DNA and to transcribe sections of DNA information into similar sequences of bases in RNA. The RNA molecules then move to other locations inside the cell where their information is translated into various series of amino acids joined together in sequences that were precisely defined in the original DNA molecule. These specifically arranged amino acids form proteins, some of which are enzymes. Enzymes, in turn, catalyze biochemical reactions that ultimately result in the growth and propagation of intact organisms. Hereditary (genetic) material can be either nucleic acids alone, as found in bacteria and viruses, or a nucleic acid in association with proteins, which form the chromosomes found in more complex organisms, including man.

Heat is a physical agent that can disrupt genetic material by causing the temperature to rise above a normal physiological range. The effect of heat, or temperature rise, has been studied in many biological systems. As examples, heat has been shown to cause: physicochemical damage in isolated DNA preparations (Lindahl and Nyberg 1974; Ginoza _et al_. 1964; Ginoza and

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Miller 1965) and in bacteria (Pellon *et al*. 1980); chromcsome changes in *Drosophila melanogaster* (Grell 1971) and in the locus (Buss and Henderson 1971), including a change from dipolid to haploid in pollen from maize (Mathur *et al*. 1980); enhanced sensitivity to other agents in mammalian cell cultures (Ben-Hur *et al*. 1974) and in *D. melanogaster* (Mittler 1979); reduced fertility in rats (Bowler 1972; Fahim *et al*. 1975); and mutations in bacteriophages (Bingham *et al*. 1976), in bacteria (Zamenhof and Greer 1958) and in *D. melanogaster* (Muller and Altenburg 1919). Because absorbed RF energy is usually dissipated as heat, all reports of genetic and mutagenic changes caused by exposure to RF radiation must be examined closely to determine whether temperature rise, or some other mechanism, is the causative agent.

Mutations are relatively permanent changes in the hereditary material involving either a physical change in chromosomal relations or a biochemical change in the sequence of nucleic acid bases that make up the genes. These changes can be passed on to future generations of cells. Two different types can be affected: germ cells, which are egg or sperm or their antecedent cells; and somatic cells, which form all other tissues in the body. Mutations in germ cells can be passed on to future generations of the organism, whereas mutations in somatic cells of an organism may lead to impairment of organ function and, in the extreme case, to cancer. Most mutations are considered harmful because they disturb the biochemical processes necessary for the survival of the organism and for the propagation of the species.

Evaluation of the mutagenic potential of RF radiation has generally followed the procedures established for testing the mutagenic activity of chemicals

(Hollaender 1971). This evaluative scheme utilizes

- Molecular systems, to detect changes in the hereditary material
- Single-cell organisms, to detect changes in structure and function that are transmissible to the next generation
- Multi-cellular systems, including plants and animals, to detect changes in reproductive potential
- Infra-human primates, to detect changes in reproductive potential

The evaluation scheme starts with simple, well-defined genetic systems that enable rapid analysis and identification of suspected agents meriting further evaluation. The more complex biological systems used in further testing require substantially larger investments of time and resources.

As discussed below, the experiments reviewed in this section have demonstrated that (1) RF irradiation of low-to-moderate intensity does not cause mutations in biological systems, and (2) the only exposures that are potentially mutagenic are those at high power densities of CW or PW radiation--exposures that result in substantial thermal loading or in extremely high electric-field forces within cells.

5.8.2 Effects on Genetic Material of Cellular and Subcellular Systems

5.8.2.1 Physical and Chemical DNA and Chromosome Studies --

Mechanisms for the absorption of RF radiation by DNA molecules are treated elsewhere in this document (see § 3.2, Mechanisms of RF-Field Interactions with Biological Systems; and § 5.1, Cellular and Subcellular Effects). This section will address the experimental studies that have examined changes in genetic material induced by RF radiation. Purified DNA or DNA extracted from the testes of exposed mice has been examined to determine if the physical properties of the molecule can be altered by the exposure to RF radiation. Hamrick (1973) examined the thermal-denaturation profiles of aqueous solutions of isolated DNA exposed *in vitro* at 37 °C to 2450-MHz (CW) radiation (SAR = 67 W/kg). No changes were found. Even elevated temperatures (to 50 °C) produced by microwaves (1 h at SAR $\leq$ 160 W/kg) did not cause a difference in the thermal denaturation profile. (See § 5.1 for details.)

Varma and Traboulay (1976) reported radiation-induced changes in thermal denaturation profiles (i.e., shift to lower temperature in the midpoint of the transition curve [Tm] and reduction in the maximum hyperchromicity) as well as changes in the base composition of testicular DNA extracted from anesthetized mice whose testes were irradiated in the near field. Ten animals were exposed individually either to 1.7-GHz radiation at 50 mW/cm^2 for 30 min (SAR estimated at 2.4 W/kg for testes alone) or at 10 mW/cm^2 for 80 min (SAR estimated at 0.48 W/kg for testes alone), or to 0.985-GHz radiation at 10 mW/cm^2 for 80 min (SAR estimated at 0.26 W/kg for testes alone). The animals exposed to 1.7-GHz fields at 50 mW/cm^2 or to 0.985-GHz fields at 10 mW/cm^2 were given a 1-day recovery period before they were subjected to euthanasia, and the DNA was extracted. The animals exposed to 1.7 GHz-fields at 10 mW/cm^2 were used in another test for 8 weeks before euthanasia, and the DNA was extracted. Identical results are reported for the 1.7-GHz exposure at 50 mW/cm^2 in another publication (Varma and Traboulay 1977); they are assumed to describe the same experiment rather than a duplicate experiment because it is unlikely that all the experimental measurements upon repetition would have given identical values. They conclude "that biological damage may be due to the combined effect of thermal and nonionizing radiation."

The experimental results reported by Varma and Traboulay must be examined with careful attention given to the control experiments and to the potential size of the thermal insult. Although the percent adenine/thymine is higher in the DNA extracted from exposed animals, which could be responsible for the drop in Tm, it is highly unlikely that identical values would be obtained for each DNA extract from the three groups of control animals. Based on the variability normally inherent in these biochemical measurements, a more probable explanation is that the control values were a pool of all the control groups or represent just one of those groups. Since the normal experimental variability in the measurements is not described--either for repeated measures on one DNA-extract preparation or between extract preparations--it is impossible to conclude that the differences cited between control and exposed samples are significant; nor can it be concluded that the differences result from the radiation exposure directly, rather than from the extraction procedures used. Similarly, the crude SAR values estimated for testicular exposures appear to be quite low to produce the types of damage cited by these authors. A more likely explanation is that the assumptions underlying either the SAR estimates or the exposure conditions are in error, and that elevated temperatures produced by the radiation exposures were the causative agent. (For example, it is possible that the temperature of the absorbing material used to shield the animals was highly elevated, and it may have elevated the testicular temperature.) In an anesthetized animal exposed in the near field to 1.7-GHz radiation at 50 mW/cm^2 for 30 min and shielded with urethane foam except for the testes (SAR estimated at 2.4 W/kg), a 1 to 2 °C rectal temperature rise was recorded following exposure (Varma and Traboulay 1977). In another report (Varma and Traboulay 1975), animals were exposed under the same conditions, except that the exposure time varied between 30 and 40 min, and the testes were examined histologically. The authors report, "the lumens were empty with complete disintegration of spermatids, Sertoli cells and the delicate connective tissue which surrounds the seminiferous tubules." In the same report, with respect to animals exposed to 1.7-GHz fields at 10 mW/cm^2, the authors state: "there was little or no damage to testes, except when the time of exposure was increased to 100 min, then severe changes in morphology were observed." There was no explanation why little or no damage suddenly became severe damage at 100 min of exposure. Anesthetized animals have been shown to lack homeothermic capacity (Cairnie _et al_. 1980). It is probable that even exposures to 10 mW/cm^2 deposited sufficient energy in these anesthetized animals to cause the temperature elevation responsible for many of the changes that are attributed to microwave-specific effects.

Thus, an evaluation of the existing evidence from physical studies on DNA indicates that RF irradiation at low-to-moderate intensities not accompanied by temperature rise causes no changes in DNA bases, the fundamental unit of the genetic code. However, if substantial elevations of temperature occur during exposure, they may cause disruptions in the pairing of the two complementary strands as well as other damage.

Other researchers have used cytogenetic techniques to examine some physical and chemical properties of chromosomes in intact cells to determine if the relationship of various parts of the genetic material is altered by RF-radiation exposure. Huang et al. (1977) reported no RF-induced chromosomal aberrations in white blood cells from Chinese hamsters exposed to 2450-MHz radiation at power densities up to 45 mW/cm^2 (SAR = 20.7 W/kg) for 15 min a day on 5 consecutive days. McRee et al. (1978) in a preliminary report found no sister chromatid exchanges in bone-marrow cells of mice exposed to 2450-MHz fields at 20 mW/cm^2 (SAR = 15.4 W/kg), for 8 h daily, 28 days total. Alam et al. (1978) showed, in great detail, that chromosomal aberrations occur in a Chinese-hamster-cell line (CHO-K1) exposed 30 min to 2450-MHz radiation from a diathermy applicator, but only if the temperature of the culture is allowed to rise to 49 °C during exposure. These authors demonstrated that irradiation of cell lines at high (> 200 mW/cm^2) power densities (SAR estimated at 360 W/kg) would cause no detectable cytogenetic effects, provided proper temperature control was maintained. Thus, heating seems to account for the observed cytological changes.

Authors of one detailed study used a frequency well below the 1.7- to 2.45-GHz range. McLees et al. (1972) exposed rats treated to undergo liver regeneration either to 13.12-MHz CW (4.45 kV_{p-p}/m) fields or to PW [44.1 kV_{p-p}/m, 200-μs pulse width, 50-Hz pulse repetition rate (PRR)] radiation for 28 to 44 h. They examined the effects of radiation on liver cell mitotic activity, that is, the percentage of cells in mitosis, and the number of chromosomal aberrations. Rat liver cells may be very sensitive to exogenous stresses during this regenerative process because they are normally nondividing cells in an intact animal that have been challenged to divide *in situ*. However, the authors found no RF-induced alterations in chromosomal morphology (SAR estimated at 1.2 to 1.3 W/kg). This result indicates that no cytogenetic changes would be expected in this range of frequencies for low-intensity exposures. Thus, although there are reports indicating that exposure to RF radiation can cause cytogenetic changes, these changes probably result from radiation-induced elevations of temperature.

5.8.2.2 Biological Studies of DNA and Chromosomes--

Bacteria have been used to study the mutagenic potential of RF radiation, because the single-cell system is simple, easy to culture, quick to test, and relatively sensitive to the action of mutagenic agents. By using the bacterial system and the biological amplification it provides for any DNA change, molecular biologists have been able to decipher the genetic code and to identify a change in as few as one DNA subunit out of 10^{10} to 10^{12} subunits. In contrast, biologists using standard physical techniques such as DNA melting curves usually can detect changes in no better than 0.1 percent of the DNA. Blackman _et_ _al_. (1976) exposed growing cultures of the bacterium _Escherichia_ _coli_ either to 1.7- or to 2.45-GHz (CW) radiation for 3 to 4 h. Exposure at 1.7 GHz was in the near field at 88 V_{rms}/m or ~ 250 V_{p-p}/m (SAR = 3 W/kg). The 2.45-GHz exposures were in the far field at either 10 or 50 mW/cm^2 (SAR = 15 or 70 W/kg, respectively). Although exposure of growing cells provided enhanced sensitivity to mutagenic agents, no mutagenic activity was detected. A positive control, ultraviolet (UV) light, caused mutations and was used to demonstrate the sensitivity of the assay method. Dutta _et_ _al_. (1979a) exposed growing cultures of various bacterial strains of _Salmonella_ _typhimurium_, commonly used in the Ames testing procedures to detect chemical mutagens (Ames _et_ _al_. 1975), to 2.45-GHz (CW) radiation for 90 min at

20 mW/cm^2 (SAR = 40 W/kg) and to 8.6-, 8.8-, 9.0-, 9.2-, 9.4-, and 9.6-GHz (PW) radiation (1-μs pulse width, 1-kHz PRR) at 10 and 45 mW/cm^2 average power densities, and 10,000 and 45,000 mW/cm^2 peak power densities. (The SAR at 45 mW/cm^2 is estimated at 80 W/kg.) No mutagenic activity was observed under any of these exposure conditions.

Another approach with bacterial systems is to test for radiation-induced alterations in genetic processes, including cell death. Since most mutations are detrimental, they might be detected indirectly by this method. Corelli et al. (1977) exposed cultures of E. coli to microwaves at frequencies swept between 2.6 and 4.0 GHz for 8 h (SAR = 19 W/kg). Although at 26 °C these cultures were probably growing slowly, no change was noted in the number of colony-forming units (CFU) in the cultures following irradiation, indicating no detectable lethal events because of the exposure. These workers also examined the infrared (IR) spectrum of these cells when exposed to 3.2-GHz radiation for 11 to 12 h (SAR is either 21 or 16 W/kg). There was no observable effect on the molecular or conformational structure of these cells, in contrast to results obtained using a positive control, ionizing radiation. Two strains of E. coli, one deficient in an enzyme needed to repair damaged DNA, were tested (Dutta et al. 1979b) for survival following microwave exposure. The exposure conditions were 8.6-GHz (PW) radiation (1-μs pulse width, 1-kHz PRR, SAR = 12 W/kg) for 1, 2, 4, or 7 h. There was no significant change in the relative growth patterns of these strains that could be attributed to microwave-induced DNA damage repairable in one strain, but not in the other. Blackman et al. (1975) exposed a different strain of E. coli in log phase (actively dividing) and in lag phase (undergoing metabolic activities preparatory to division) at 32 °C for 4 h to 2.45-GHz radiation at 0.005, 0.5, 5.0, or 50 mW/cm^2 (at 50 mW/cm^2 power density the SAR = 75 W/kg). Additional experiments were conducted at 5 mW/cm^2 and 25 °C to test for the influence of cold stress, and in two-culture media at 30 and 35 °C to compare the relative influence of a rich medium with a minimal medium, the latter requiring greater utilization of the genetic apparatus of the cell for growth to occur. They found no change in the colony-forming ability of the cultures due to the exposure except for enhanced growth at 50 mW/cm^2, which was attributed to slight temperature rises in the exposed cultures.

Few researchers have used single-cell systems more complex than bacteria specifically to look for RF-radiation-induced mutagenesis. Dutta _et_ _al_. (1979a) exposed a diploid strain of the yeast _Saccharomyces_ _cerevisiae_, a primitive eukaryote, to 2.45-GHz (CW) radiation for 2 h at 20 mW/cm^2 (SAR = 40 W/kg). They found essentially no change in the number of mutations at either of two loci affecting the nutritional requirements for adenine or tryptophan. These investigators conducted additional tests at 8.5-, 8.6-, 8.8-, 9.0-, 9.2-, 9.4-, and 9.6-GHz (PW) radiation (1-μs pulse width, 1-kHz PRR) for 2 h at average power densities of 1, 5, 8.9, 10, 15, 30, 35, 40, or 45 mW/cm^2. Although no measurements of SAR are cited, thereby making comparisons with CW exposures difficult, the highest power density was reported to raise the temperature of the culture by 12 °C, indicating substantial absorption of the radiation. (At 45 mW/cm^2 power density the estimated SAR = 80 W/kg). In no case did the exposures cause a change in the frequency of genetic events, altering the requirements for either adenine or tryptophan, in the treated population as compared with the control population. Dardalhon _et_ *al*. (1980) exposed a diploid strain of *S. cerevisiae* at 20 °C in the near field of 9.4-GHz (CW) radiation (SAR estimated at < 2) for 1 to 5 h, or in the near field of 17-GHz (CW) radiation at either of two power densities (SAR's estimated at 28 or < 6 W/kg, respectively) for various times to 24 h. No significant changes attributable to the irradiation were observed in the percent survival, in the induction of cytoplasmic "petite" mutations, in the induction of mitotic recombinations, or in sporulation. Thus, no changes were detected in complex single-cell systems used to examine directly the mutagenic potential of microwaves.

Some work has been done with bacteria and yeast cultures that compares the lethal and mutagenic effects of microwaves with those induced by conventional heating. Dutta *et al*. (1980) examined the responses of various strains of the bacteria *S. typhimurium* and *E. coli* and those of a diploid strain of the yeast *S. cerevisiae*, exposed to 8.6-, 8.8-, or 9.0-GHz (PW) radiation (1-kHz PRR, 1-μs pulse width) at average power densities to 45 mW/cm^2 (SAR estimated maximum at 80 W/kg). The bacteria were exposed 90 min at an ambient temperature of 37 °C, whereas the yeast was exposed 2 h at 30 °C. The results of these irradiation treatments were compared with those obtained from treatments at elevated temperatures produced by conventional heating. The comparison indicated that conventional heating could produce cellular damage leading to reduced survival in a manner similar to the changes caused by microwave-induced elevations of temperature (to 10 °C above normal growth temperatures). No mutational events occurred in bacteria to 42 °C, or in the yeast to 40 °C; however, at 45 °C, a slight increase in mutational events occurred in the yeast, and at 47 °C, in *S. typhimurium*.

Dardalhon *et al*. (1980) exposed a diploid strain of *S. cerevisiae* for 3 h at 52 °C. (Normal growth temperature is 30 °C.) Large changes were observed in the percent survival, in the induction of cytoplasmic mutations, and in the induction of mitotic recombinations after 3 h, compared to no changes in these end points during microwave exposure at 20 °C to 9.4-GHz or 17-GHz fields (SAR estimated at < 28 W/kg), described above. Both groups of authors conclude that care must be exercised in evaluating genetic changes in microbial assay systems when elevated temperatures accompany microwave exposure.

5.8.3 Effects on Genetic Material of Higher-Order Biological Systems

5.8.3.1 Plants--

Plant systems are sensitive to mutagenic agents and thus can serve to identify conditions that should be examined more carefully in mammalian systems. Although there are several studies reported in the literature, none has sufficiently described experimental conditions to allow independent evaluation of the work. Thus, useful mutagenic testing of RF radiation with respect to plant systems has yet to be accomplished and documented.

5.8.3.2 Invertebrates--

Several investigators have studied *D. melanogaster*, a standard model for testing mutations induced by RF radiation. No mutagenic effects were reported by Hamnerius *et al*. (1979) in embryos exposed 6 h in water at 24.5 °C to 2450-MHz (CW) fields at 100 W/kg. Similar negative effects were reported by Pay *et al*. (1972), who exposed adult males to 2450-MHz fields for 45 min at 4600, 5900, or 6500 mW/cm^2 (SAR's estimated at 140, 190, and 210 W/kg, respectively) and mated each of the surviving males individually with two virgin females during 15 consecutive days. No changes were observed in the generation time or sex-ratio pattern of the offspring. These offspring were then mated and observed for possible sex-linked lethal mutations in their offspring. No such mutations were found at frequencies > 1 percent, a detection limit based on the small number of chromosomes (< 800) actually evaluated. An additional caveat by the authors was that the most sensitive stages to detect recessive sex-linked lethal mutations, late spermatocytes and early meiosis, were not tested in their study, because few sperm were still in meiosis at the time of exposure. Mittler (1976), who exposed adult males from various strains of _D_. _melanogaster_ to 29-MHz (CW) fields at 600 V_{rms}/m (SAR roughly estimated at 0.024 W/kg) and to 146-MHz (CW) fields at 62.5 V_{rms}/m (SAR roughly estimated at 0.015 W/kg) for 12 h, mated them with virgin females for 12 h every 2 days in production of 4 or 5 broods. In these experiments, brood 4 was produced from sperm irradiated "in or about meiosis." There were no mutations induced by these treatments as evidenced by the lack of chromosome loss, nondisjunction, or sex-linked recessive lethals. In addition, Mittler (1977) observed no mutagenic effects (recessive lethals) when exposing adult females to 98.5-MHz frequency-modulated fields (composed of standard commercial broadcast audio frequencies) at 0.3 V_{rms}/m (SAR estimated at 0.0004 W/kg), 134 h per week for 32 weeks. Although the results with _D_. _melanogaster_ are difficult to extrapolate to the human condition, this test system as a qualitative index was not able to detect any mutagenic alterations by RF radiation over a wide range of frequencies.

5.8.3.3 Vertebrates--

Experiments with vertebrates address the impact of the genetic effects of RF radiation most directly because of the general biological similarities between man and other vertebrates. However, there are very few such experiments directed at this subject. Three studies have been reported that are directly focused on the mutagenic potential of microwaves in mice and rats. Varma et al. (1976) used the dominant-lethal test to investigate the effects of 2.45-GHz (CW) radiation. The testes of anesthetized mice were treated either by a single 10-min exposure at 100 mW/cm^2 (SAR estimated at 11.4 W/kg), or by three exposures of 10 min each at 2-h intervals on the same day at 50 mW/cm^2 (SAR estimated at 5.7 W/kg), or by four exposures of 10 min each at 3-day intervals over 2 weeks at 50 mW/cm^2 (SAR estimated at 5.7 W/kg). Varma and Traboulay (1976) in a similar study exposed the testes of anesthetized mice to a single dose of 1.7-GHz radiation, at 10 mW/cm^2 for 80 min (SAR estimated at 0.48 W/kg) or at 50 mW/cm^2 for 30 min (SAR estimated at 2.4 W/kg). Following a 24-h recovery period, the males were bred with virgin females--one group of females per week for 6 to 8 weeks. In the 2.45-GHz study, the authors used the week-6-group results for comparison; they found a higher mutagenicity index in the results of the 100-mW/cm^2 group bred at week 1, and in the results of the 50 mW/cm^2 group exposed three times in one day and bred at week 4. The authors concluded that a single, intense exposure or multiple exposures during one day induced a number of significant mutations in the mice. The results of the 1.7-GHz studies at 50 mW/cm^2 for 30 min indicated a radiation-induced increase in infertility, in pre-implantation losses, and in the mutagenicity index of the groups bred at 3, 4, 5, and 6 weeks. In addition, for the group exposed to 1.7-GHz fields at 10 mW/cm^2 for 80 min, an increase was seen in the mutagenicity index of the groups bred at 1, 2, 3, and 6 weeks. The authors concluded that the "biological damage may be due to the combined effect of thermal and nonionizing radiation." Both of these reports should be evaluated on the basis described in § 5.8.2.1, Physical and Chemical DNA and Chromosome Studies, for the physical and chemical studies reported by these authors. It is not possible to determine the extent of the biological damage caused by elevated temperature in either of these reports, especially because anesthetized mice lack an effective temperature-regulation capability (Cairnie et al. 1980). However, if the histological damage found in the testes of animals exposed under similar conditions (Varma and Traboulay 1975) is reflected in damage to sperm, it could account for many if not all of the changes in the mutagenic index, fertility, and pre-implantation loss reported by those authors in later studies.

The conclusion that radiation in this frequency range could cause mutagenic changes in mice was challenged in a detailed study by Berman et al. (1980), who exposed unanesthetized male rats to 2.45-GHz (CW) radiation under three treatment regimens: 4 h/day from day 6 of gestation to 90 days of age at 5 mW/cm^2 (SAR varied from 4.7 W/kg to somewhat less than 0.9 W/kg at day 90, because growth of the animals changed their energy absorption efficiencies), 5 h/day for 5 days beginning on day 90 at 10 mW/cm^2 (SAR estimated at 2 W/kg), and 4 h/day, 5 days/week, for 4 weeks beginning on Day 90 at 28 mW/cm^2 (SAR estimated at 5.6 W/kg). During selected weekly periods after treatment, the exposed males were bred to untreated females that were examined in late pregnancy by the dominant-lethal assay. No significant germ-cell mutagenesis was detected under any treatment condition, even though significant increases in rectal and testicular temperature were observed during the 28-mW/cm^2 exposure and were associated with a concomitant decrease in incidence of pregnancy during some of the breeding periods, which indicates temporary sterility. In addition, these authors reexamined the data of Varma and concluded they had been interpreted incorrectly because the effects of litter size on fetal mortality had been ignored and the differences between treated and control groups had been overemphasized when the control values were not representative of normal values. Berman et al. (1980) concluded "it still remains to be demonstrated that microwaves, even at near-lethal doses, can cause a dominant lethal mutagenic effect in the mouse or the rat." Thus, well designed experiments with biological systems having complex genomes similar to man's have demonstrated no mutagenic effects from low- to moderate-intensity RF radiation when the temperature of the biological system is maintained in the physiological range. Most of the reported changes are consistent with the effects expected from elevations in temperature, caused by CW exposure to high-intensity RF radiation. The other changes cited in this section may result from incomplete experimental design.

5.8.4 Unresolved Questions

Heating, which raises the temperature of biological samples above normal physiological ranges and may result in genetic and mutagenic changes, is a well known result of exposure to high-intensity RF radiation. The choice of exposure conditions to study the genetic and mutagenic effects of moderate- to low intensity radiation is arbitrary because no other well defined mechanism of RF interaction has been developed to address this biological problem. The experimenter must select the frequency, intensity, and duration of exposure, as well as the type and characteristics of modulation. To compound the problem further, there are an almost limitless number of biological systems that could be selected for study. There are several guides that can be developed from recent experimental findings to help delineate a future experimental plan.

Although the conclusion has been stated above that no strong evidence exists in the cited reports to demonstrate mutagenic activity for low intensity RF radiation per se, it should be qualified by the following observations:

1. These experiments are limited to small portions of the RF region of interest, i.e., 0.5 MHz to 100 GHz. This 10^6-Hz frequency range is so large that if detrimental effects occurred over very narrow frequency ranges, they might have gone undetected.
2. Many of the experiments were conducted with CW radiation. If effects exist, they may occur with amplitude-, frequency-, or PW-modulated radiation at frequencies associated with ongoing biological or biochemical processes. An exposure to a short-duration, high-intensity PW radiation (radar-like) may not produce the same biological response as a CW exposure of the same average power density. Thus, the concept of averaging the intensity of PW radiation over time to determine an effective intensity may not be generally valid.
3. The general approach in most experimental studies has been to assume that the higher the radiation intensity, the more pronounced the biological effect. It is possible that several mechanisms are operative during radiation exposure and that mechanisms with thresholds at relatively high intensities (e.g., heating) mask the effects being caused by the more subtle mechanisms.
4. RF radiation, as a co-stressor, may enhance the effects of known mutagenic agents. In environmentally relevant situations, biological systems are exposed simultaneously to many agents, both chemical and physical.
5. Since no mechanism has been developed to describe the interaction of RF radiation with complex biological structures and genetic material, it could be argued that standard procedures that have been optimized to identify ionizing and chemical mutagens are not necessarily applicable to this form of radiation. Thus, in view of this lack of knowledge, no test system should be overlooked

as potentially sensitive for detection of mutagenic activity. For example, plant systems have been shown to be extremely sensitive indicators of environmental pollution.

Recent experimental developments support some of the suggestions made above. Possible frequency-specific responses were reported by Smolyanskaya and Vilenskaya (1973), who described the induction of colicin in *E. coli* by extremely high-frequency radiation, near 37 GHz, at power densities of 0.001, 0.01, 0.1, or 1.0 mW/cm^2 for 0.5, 1, and 2 h. Colicin is a protein usually not made by the cell. Its induction, while not well understood, requires the transcription of a new portion of the DNA molecule. This induction demonstrates that specific microwave frequencies can induce changes in the genetic processes of cells. More recently, Grundler *et al*. (1977) described frequency-dependent growth responses in the yeast *S. cerevisiae* exposed for periods to 11 h to microwave frequencies between 41 and 42 GHz at 1 to 3 mW/cm^2 (average SAR estimated at 4 to 11 W/kg). (See § 5.1, Cellular and Subcellular Effects, for details.) Although this work is controversial, it supports the frequency-specific-response concept.

The importance of examining the effects of RF radiation as a co-stressor with other agents is emphasized in the report by Dardalhon *et al*. (1980) that was discussed earlier with respect to exposure either to heat or to microwave radiation. These authors exposed haploid and diploid strains of *S. cerevisiae* for 1 h to 17-GHz (CW) radiation, near field, at 50 mW/cm^2 (SAR estimated at < 6 W/kg) and 20 °C, followed by exposure to various doses of UV light (254 nm), which is known to cause damage directly to the DNA. Both haploid and diploid strains were affected. The exposure combination caused a tendency--

but apparently not a statistically significant change--toward diminished survival, increased mitotic recombination, and increased cytoplasmic "petite" mutations, when compared with the effects caused by exposure to the same doses of UV light alone. This microwave-radiation enhancement of effects due to UV-light exposure is unusual, because enhancement was observed only at high doses of UV light, where, presumably, additional repair systems are operative. Similar trends were obtained by replacing microwave-radiation exposure with temperature elevation to 46 °C before treatment with UV light. No influence from exposure to microwave radiation, followed by UV light, was observed for 17-GHz fields at 2.5 mW/cm^2, or for 9.4-GHz fields at 5 mW/cm^2. Because the microwave-radiation treatment caused only a 1 °C global temperature rise in the sample that was 10 °C below its normal growth temperature, the authors reasoned that if temperature rise is the basic agent enhancing the UV-light-induced response, it must be occurring selectively at specific sites within the biological system other than on the DNA itself, causing change perhaps in metabolic processes or in the structural integrity of cytoplasm, or of membranes. In this case, there may be a differential sensitivity among the various repair systems induced by the UV light. This type of investigation potentially can reveal biological processes, including repair of damage or detoxification of chemicals, that may be particularly sensitive to microwave-radiation exposure.

In another area, radiation-induced efflux of calcium ions from *in vitro* brain tissues has been shown to depend on the modulation frequency of a carrier wave (Bawin *et al*. 1975; Blackman *et al*. 1979). The effective modulation frequencies were in the same frequency range as the natural biological rhythms associated with the EEG in the intact animal, and thus the radiation may have coupled with an existing oscillatory system. Further studies by Blackman et al. (1979; 1980a,b) and Sheppard et al. (1979) indicated that higher and lower intensities of radiation can lead to the disappearance of the effect. This suggests that examining biological processes only at a single power density may provide misleading information.

Three additional, incomplete reports have been included in this section. These studies are included either because they present positive findings at frequency ranges or intensities seldom studied or because of a strong claim of the authors. Heller (1970) and Mickey and Koerting (1970) reported chromosomal aberrations in cultured Chinese-hamster-lung cells exposed for 30 min to 19- or 21-MHz fields, although no changes were observed after exposure to 15- or 25-MHz (PW) fields (100-Hz PRR, 50-μs pulse width) at field intensities to 300 kV_{p-p}/m. It is very likely either that the extremely high peak voltages (up to 300 kV_{p-p}/m) were producing intense, rapid heating within the cells, or that the field per se was causing major stresses within the system. These reports provide insufficient descriptions to allow an estimate of the SAR values, and, thus, these results cannot be compared with those found by others. It is possible that fields at extremely high intensities can account for some cytogenetic changes. Manikowska et al. (1979) reported a non-dose-dependent increase in chromosomal translocations and in chromosomal pairs remaining as univalents at Metaphase I in the sperm cells of mice exposed 1 h/day, 5 days/ week, for 2 weeks to 9.4-GHz (PW) radiation at 200-, 1000-, 2000-, or 20,000 mW/cm^2 peak power densities (0.5-μs pulse width; 1-kHz PRR; 0.1-, 0.5-, 1-, and 10-mW/cm^2 average power densities, respectively). (Average SAR is roughly estimated at 5 W/kg, and peak SAR roughly at 9000 W/kg for the highest power density used.) The authors do not describe the relation of the animals' testes to the incident field, thereby raising the question of the actual quantities of energy coupled to the target cells at 9.4 GHz, where tissues exhibit large attenuation coefficients. A description of the environmental conditions during exposure is also absent. These omissions essentially prevent any critical assessment of the results. Furthermore, because of the small number of animals used in the study, the authors state that "the findings ... obviously need confirmation on larger numbers of animals."

In another study, based on bacteria exposed to extremely high temperatures, an incomplete analysis of the distribution of temperatures within the samples led to an unjustified conclusion. Blevins et al. (1980), who exposed several strains of S. typhimurium commonly used in the Ames testing procedures (Ames et al. 1975) to 2.45-GHz radiation in a microwave oven at a calculated power density of 5100 mW/cm^2 for periods of 2 to 23 s, examined the cultures for lethality and for mutation induction. These exposures caused extremely large elevations of temperature. Corollary heating experiments were performed in high-temperature water baths to determine the extent to which temperature change alone contributed to lethality and mutations. Their conclusion that microwave radiation is a potent mutagen was not supported by their data, because the authors failed to demonstrate that the uniformity of microwave heating was duplicated by the water bath experiments. The authors acknowledge that "differences in the kinetics of water bath and microwave heating are possible" but fail to evaluate this possibility further. Because of the large temperature increases in their culture systems--apparently as large as

46 °C in 14 s, more definitive temperature distribution work must be done to establish accurately the contribution that temperature change makes to induction of mutations before additional mutagenic properties are assigned to microwaves. Blevins et al. (1980) reported using a power density 500 times greater than the current U.S. occupational guidelines, and, because the apparent mechanism is based on such high, nonphysiologic temperatures, the authors' conclusions are not applicable to the other cited studies, which have used 2.45-GHz radiation. However, the study may support a reevaluation of the concept that brief, high-intensity exposures can be averaged over a longer time period to define the average intensity. For example, an exposure to 5100 mW/cm^2 for 2 s is 28 mW/cm^2 if averaged over 6 min, and an exposure for 14 s becomes 200 mW/cm^2 if averaged over 6 min. The Blevins et al. study would also support the concept that high-intensity pulses of microwaves may affect biological systems differently from convection or conduction heating.

Although no solid evidence exists (i.e., there are no independently verified reports) to indicate that low-intensity RF radiation is mutagenic, sophisticated concepts and designs are just beginning to appear in experiments concerning the biological effects of RF radiation. Thus, although it is premature to proclaim unequivocally that RF radiation is not mutagenic, the vast majority of evidence presently indicates that in the absence of temperature elevation this statement is true. The above studies of the biological effects of RF radiation that relate to genetics and mutagenesis are summarized in Table 5-21.

TABLE 5-21. SUMMARY OF STUDIES CONCERNING GENETIC AND MUTAGENIC EFFECTS OF RF-RADIATION EXPOSURE

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm^2)	Duration (days x min)	SAR (W/kg)	
No change in thermal denaturation profile, except at elevated temperature	DNA	2450 (CW)	134	1 x 960	67 (est)*	Hamrick (1973)
Change in thermal denaturation profile and hyperchromicity of DNA extracted from testes following exposure	Mouse	1700 (CW) 985 (CW)	$\leq$ 50 $\leq$ 10	1 x 80	$\leq$ 2.4 (est) $\leq$ 0.26	Varma and Traboulay (1976, 1977)
No chromosome aberrations in white blood cells	Chinese hamster	2450 (CW)	5-45	5 x 15	21	Huang _et al_. (1977)
No sister chromatid exchange in bone marrow cells	Mouse	2450 (CW)	20	28 x 480	15	McRee _et al_. (1978)
No chromosome aberrations in CHO-K1 cell line if temperature maintained	Chinese hamster	2450 (CW)	$\leq$ 200	1 x 30	$\leq$ 360 (est)	Alam _et al_. (1978)
No chromosome aberrations or change in mitotic activity in regenerating liver cells in rat	Rat	13.12 (CW) 13.12 (PW)	4.45 kV_{p-p}/m 44.1 kV_{p-p}/m	1 x 1680-2640	1.3 (est)	McLees _et al_. (1972)
No mutation induction	_E. coli_ _E. coli_	2450 (CW) 1700 (CW)	10 or 50 250 V_{p-p}/m	1 x 180-240 1 x 210	15 or 70 3	Blackman _et al_. (1976)
No mutation induction observed in Ames tester strains	_S. typhimurium_	2450 (CW) 8600-9600 (PW)	20 10, 45	1 x 90 1 x 90	40 18, 80 (est)	Dutta _et al_. (1979a)

(continued)

TABLE 5-21. (continued)

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
Reduction in survival concomitant with rise in sample temperature	*E. coli*	8600-9000 (PW)	1-20	1 x 90	≥ 50	Dutta *et al*. (1980)
	S. typhimurium *S. cerevisiae*	8600-9000 (PW) 8600-9000 (PW)	≤ 45 ≤ 45	1 x 90 1 x 120	≤ 80 ≤ 80	
No reduction in survival or mutational events	*S. cerevisiae*	9.4 (CW) 17 (CW)		1 x 300 1 x 1440	≤ 28 (est)	Dardalhon *et al*. (1980)
No detectable lethal events due to no change in CFU's	*E. coli*	2600-4000 (CW)		1 x 480	19	Corelli *et al*. (1977)
No observable change in molecular structures because no change in IR spectrum	*E. coli*	3200 (CW)		1 x 660-720	21 or 16	Corelli *et al*. (1977)
No repairable DNA damage	*E. coli*	8600 (PW)		1 x 60-420	12	Dutta *et al*. (1979b)
No change in growth pattern; enhanced colony-forming activity	*E. coli*	2450 (CW)	0.005-50	1 x 240	0.008-75	Blackman *et al*. (1975)
No change in mutation frequencies at either of two loci controlling requirements for adenine and tryptophan	*S. cerevisiae*	2450 (CW) 8500-9600 (PW)	20 1-45	1 x 120 1 x 120	40 ≤ 80 (est)	Dutta *et al*. (1979a)
No mutagenic effects in exposed embryos	*D. melanogaster*	2450 (CW)	--	1 x 360	100	Hamnerius *et al*. (1979)
No changes in generation time, sex ratio, or sex-linked lethal mutations in offspring	*D. melanogaster*	2450 (CW)	4600-6500	1 x 45	150-210 (est)	Pay *et al*. (1972)
No mutations in adult males as evidenced by chromosome loss; nondisjunction; or sex-linked recessive lethals	*D. melanogaster*	29 (CW) 146 (CW)	$600\ V_{rms}/m$ $62.5\ V_{rms}/m$	1 x 720 1 x 720	0.024 (est) 0.015 (est)	Mittler (1976)

(continued)

TABLE 5-21. (continued)

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
No mutagenic changes (recessive lethals) in adult females	D. melanogaster	98.5 (CW)	0.3 V_{rms}/m, (FM) at audio	224 x 1140	0.0004 (est)	Mittler (1977)
No significant germ-cell mutagenesis in weekly breedings	Rat	2,450 (CW)	5	106 x 240	4.7-0.9	Berman et al. (1980)
No significant germ-cell mutagenesis in weekly breedings	Rat	2,450 (CW)	10	5 x 300	2	Berman et al. (1980)
Same, except decrease in pregnancies, indicating temporary sterility caused by elevated testicular temperatures	Rat	2,450 (CW)	28	20 x 240	5.6	Berman et al. (1980)
Induction of a repressed protein, colicin, indicating a change in the genetic processes	E. coli	37,000 (CW)	0.001-1	1 x 30-120		Smolyanskaya & Vilenskaya (1973)
Change in growth rate that was very frequency specific, indicating an alteration in the processes of the cell	S. cerevisiae	41,000-42,000 (CW)	1-3	1 x 660	4-11 (est, av)	Grundler et al. (1977)
Chromosome aberrations in lung cells in vitro at two frequencies but not at two closely related frequencies, 15 or 25 MHz	Chinese hamster	19 (PW) 21 (PW)	up to 300 kV_{p-p}/m	1 x 30		Heller (1970) Mickey and Koerting (1970)
Increase in chromosome translocations in sperm cells	Mouse	9,400 (PW)	0.1-10	10 x 60	0.05-5 (est)	Manikowska et al. (1979)
Increased mutations and lethality	S. typhimurium	2,450 (CW)	5100	1 x 0.03-0.48		Blevins et al. (1980)

*est = estimated; av = average.

5.9 LIFE SPAN AND CARCINOGENESIS

William P. Kirk

5.9.1 Life Span

There are few data (Table 5-22) and no definitive studies on which to judge the effects of RF-radiation exposure on human longevity. Pazderová-Vejlupkova and Josifko (1979) mention some previous studies in which various clinical parameters were examined in 82 employees of radio transmitting stations (0.3 to 30 MHz; 14.4-year mean exposure; mean intensity = 80 V/m) and 58 employees of TV transmitting stations (30 to 300 MHz; 7.2-year mean exposure; mean intensity = 2.9 V/m). No signs of damage were found in these personnel; however, the study did not directly address mortality. More recently, information has been developed on the mortality experience of U.S. Government employees assigned to the Moscow Embassy during the period 1953 to 1976, when Soviet microwave irradiation of the U.S. Embassy was taking place. Comparisons were made with a group of employees who had been stationed at other U.S. Embassies in Soviet Bloc cities (Budapest, Leningrad, Prague, Warsaw, Belgrade, Sophia, and Zagreb). The comparison group was chosen to be as similar as possible to the 1800 employees in the Moscow group for selection (i.e., posting) criteria and environmental influences, except that the posts were not subject to microwave exposure (Lilienfeld et al. 1978). Exposures to 2.56- to 4.1-GHz radiation at a maximum power density of 5 $\mu W/cm^2$ were documented from August 1963 to May 1975; the frequency range was expanded to 0.6 to 9.5 GHz in May 1975, and the maximum power density was increased to 18 $\mu W/cm^2$ from August 1975 to February 1976. The duration of exposure ranged from 0.5 h/day to 20 h/day (United

TABLE 5-22. SUMMARY OF STUDIES CONCERNING RF-RADIATION EXPOSURE EFFECTS ON LIFE SPAN/CARCINOGENESIS

Effects	Species	Exposure Conditions				References
		Frequency (MHz)	Intensity (mW/cm²)	Duration (days x min)	SAR (W/kg)	
No effect on life span or cause of death	Human adult male & female	2560-4100 600-9500	0.005 (max) 0.018 (max)	8030* x 600 180 x 1200	2×10^{-4} (max) 7×10^{-4} (max)	Lilienfeld *et* *al*. (1978)
No effect on mortality in a military population followed for 20 years	Human adult male	200-5000 (est) (PW)	~ 1 (routine) 100 (occasional)	730 x 480 (est)	<0.05 (est) ≤5 (est)	Robinette *et* *al*. (1980)
Slight increase in mean life span	Adult mouse	800	43	175 x 120	12.9 (est)	Spalding *et* *al*. (1971)
Increased mean and maximum life span for "irradiated mice with tumors." Increased mean life span but no change in maximum life span of non-tumor-bearing mice. Delay in development of tumors in irradiated mice but no change in ultimate number of tumors	Infant mouse	2450	-	4 x 20 (*in* *utero*)	35	Preskorn *et* *al*. (1978)
Increased mean life span in irradiated mine (concurrent infection-pneumonia)	Adult mouse	9270 (PW)	100	4.4 min/day 5 days/week 59 weeks	40 (est)	Prausnitz and Süsskind (1962)

*The duration of 8030 days equals the number of years (22) of irradiation of the embassy and length of the study period, but the average exposure of individuals is estimated to be 2 to 4 years.

States Senate Committee on Commerce, Science, and Transportation 1979). No evidence was found that the Moscow group had experienced any higher mortality or any differences in specific causes of death up to the time of the report. However, investigators noted that, because the population was relatively young, it is too early to detect long-term mortality effects except for those serving in the earliest period of the study. This important study is covered in more detail in § 5.10 Human Studies.

Robinette et al. (1980) examined the records of a group of 40,000 U.S. Navy personnel who enlisted during the period 1950 to 1954. Approximately 20,000 had job classifications with maximum potential for exposure to radar (i.e., electronics technicians, fire control technicians, and aviation electronics technicians). A similar number of radio and radar equipment operators believed to have a minimal potential for exposure were used as a comparison group. No specific data on exposure or frequencies were provided; however, the authors state that the low exposure group of radio and radar operators were exposed to levels well below 1 mW/cm^2, whereas the high exposure occupations involved average exposure levels below 1 mW/cm^2 during duty hours combined with infrequent higher exposures, which on occasion may have exceeded 100 mW/cm^2. The authors found no apparent difference in the long-term mortality patterns between the two exposure groups more than 20 years post exposure. This study is also covered in more detail in § 5.10.

Although there have been many experiments to determine the lethal effects in animals exposed to high levels of RF radiation, data on life span effects of experimental animals exposed to low power levels are scarce. To our knowledge there is only one report of a study in which animals were exposed to microwave radiation as the sole stressor and observed throughout their life span. Spalding et al. (1971) exposed 24 adult female mice to 800-MHz fields at a power density of 43 mW/cm^2, for 2 h/day, 5 days/week for 35 weeks. A waveguide apparatus was used to irradiate the animals, which were cooled by forced air. No temperature or relative humidity data are reported. The whole-body-averaged SAR is estimated to be 12.9 W/kg. Four exposed mice died of "thermal effects" during the experiment, and a fifth is reported to have died during exposure because it became too obese for the exposure chamber. The mean life span of the remaining 19 exposed mice was 664 ± 32.2 (SEM) days, while that of the 24 sham-irradiated mice was 645 ± 32.2 (SEM) days.

Prausnitz and Süsskind (1962) studied pathological and longevity effects on male Swiss mice exposed to 9270-MHz (PW) radiation (duty cycle = 0.001) at an average power density of 100 mW/cm^2 for 4.5 min daily, 5 days/week for 59 weeks. The daily exposure produced an average body temperature rise of 3.3 °C. This daily dose is stated to be half the LD_{50} for the mice. Originally there were 200 irradiated mice and 100 control mice. Five percent of each group was killed for pathological and hematological examination 7 months after the beginning of irradiation, and an additional 10 percent of each group was killed at 16 months. The latter series was done within a month of the final irradiation. Because of a partial contradiction in pathological findings in the animals killed at 7 and 16 months, all surviving mice (19 controls and 67 irradiates) were killed 19 months after the beginning of irradiation (4 months after final irradiation). The data from this experiment are summarized in Table 5-23. The authors state that the longevity of the mice did not appear to

TABLE 5-23. SUMMARY OF PRAUSNITZ AND SUSSKIND DATA (1972)

Series	When Sacrificed (months)	Controls (100 total)				Irradiates (200 total)				Comment
		No. Animals	% of Total	No. with "Leucosis"	% This Series with "Leucosis"	No. Animals	% of Total	No. with "Leucosis"	% This Series with "Leucosis"	
Sacrifice Series #1	7	5	5	None apparently given	--	10	5	None apparently given		Reported as negative for "leucosis"
Sacrifice Series #2	16 (1 month post-irradiation)	10	10	1	10	20	10	6	30	Reported as positive for "leucosis" Not statistically significant χ^2 (1 df) = 1.49
Sacrifice Series #3 (all animals surviving at 19 months)	19 (4 months post-irradiation)	19	19	4	21	67	33.5	12	18	Reported as negative for "leucosis"
Longevity Series	As occurred	40	40	4	10	60	30	21	35	See text
Spontaneous Deaths	No data given	26	26	--	--	43	22	--	--	Autolysis too advanced for diagnosis of cause of death

be affected under the prevailing conditions. The data appear to support a stronger statement, i.e., significantly more irradiated mice than controls survived until the termination of the experiment 19 months after the beginning of irradiation.

The difference in survival is not statistically significant at 14 months into the experiment ($\chi^2 \sim 2.2$, using data from Fig. 3, Prausnitz and Süsskind 1962) but is significant at 19 months ($\chi^2 = 4.9$, $0.05 > P > 0.025$). The data provided are not sufficiently detailed to apply more refined methods of analyzing survival (Peto et al. 1976, 1977). The authors suggested that, in view of problems with pneumonia experienced in both control and irradiated mice in the last few months of irradiation, "conceivably microwave irradiation in this modality, with periodically induced slight artifical fevers, is of some benefit to the animal in combatting disease."

There have been some reports of altered and possibly enhanced immunological competence after microwave exposure. These are discussed in detail in § 5.2, Hematologic and Immunologic Effects. In a relevant study, Preskorn et al. (1978) compared tumor development and longevity in female mice prenatally exposed to 2450-MHz microwaves with sham-irradiated controls. The irradiated mice were offspring of dams exposed for 20 min/day on days 11, 12, 13, and 14 of gestation in a multimodal cavity (SAR = 35 W/kg). Both groups were injected with sarcoma cells at age 16 days. Both the mean and maximum survival time of "irradiated mice with tumors" exceeded those of "non-irradiated mice with tumors" ($P < 0.05$). The mean survival time of "irradiates without tumors" was also greater than "non-irradiated mice without tumors." When 50 percent of the controls had died, 67 percent of the irradiates were alive. The difference was not significant ($0.05 < P > 0.1$), however, and maximum life span did not differ.

Rotkovska and Vacek (1972, 1977) reported increased survival and increased LD_{50-30} in mice for sublethal (600 to 750 R) acute exposures to 200 kV x-rays if the x-ray exposures were preceded (1, 3, 14 days) or followed (30 min) by a 5-min exposure to 2450-MHz microwaves at 100 mW/cm^2. In their initial experiment, the 30-day survival after a 600-R x-ray exposure was increased from 14 percent (controls) to 53, 88, or 90 percent when such exposure followed the microwave irradiation by 1, 3, or 14 days, respectively. In their second experiment, the LD_{50-30} was increased by 100 R with all microwave-irradiated groups having significantly higher survival at 30 days than their control counterparts. These data illustrate the plethora of potentially confounding variables that may have to be considered in determining RF-radiation exposure effects.

5.9.2 Carcinogenesis

Carcinogenesis is the process of inducing cancer or malignant neoplasia. Neoplasia is uncontrolled growth or cell division in a tissue and is considered malignant if cells from the affected tissue (tumor) enter the blood and travel to other parts of the body to colonize and form new tumors (metastases). A tumor that does not metastasize is considered benign, although it may well grow to sufficient size to be life-threatening. Consideration of the various theories of carcinogenesis is beyond the scope of this discussion, except to note that most authorities believe that the initiating event on the cellular level involves physical or chemical alterations of a cell such that its descendent cells are abnormal and may override the body's cellular proliferation control processes. The role that the immune system plays in primary carcinogenesis has not been well documented and is somewhat controversial. However, it is thought that neoplasia may arise through an epigenetic mechanism in which immunosuppression allows the development of tumors initiated by a genetic event.

The specter of potential carcinogenicity has been periodically raised in connection with RF-radiation exposure since 1953, when J. R. McLaughlin, a medical consultant to the Hughes Aircraft Corporation, submitted a report to the military, listing leukemia as one of the possible effects of radar exposure (McLaughlin 1953). The relevant literature, which is sparse, has been reviewed by Baranski and Czerski (1976), Justesen et al. (1978), and Dwyer and Leeper (1978) with little supportable evidence that RF exposures are likely to be carcinogenic. However, the subject remains controversial for many reasons, including

(1) Widespread fear of cancer in large segments of the population

(2) The proven carcinogenicity of ionizing radiation

(3) The failure of the public and the media to distinguish between ionizing and nonionizing (i.e., RF) radiation

(4) The existence of several anecdotal reports of association of cancer with RF-radiation exposure in humans

(5) The publication of an early animal study (Süsskind 1962, Prausnitz and Süsskind 1962) reported by the authors to show leukemogenesis in mice chronically irradiated with microwaves

(6) The unsupported reports by Zaret (1976) of an increased incidence of cancer in North Karelia followed by the misinterpretation of

the Zaret article by Dwyer and Leeper (1978), coupled with their editorial transformation of the North Karelia Project from a study of cardiovascular disease to a study of cancer

(7) The recent reports by Szmigielski et al. (1980) that exposure to 2450-MHz microwaves accelerated the development in mice of spontaneous breast cancer and 3,4-benzopyrene-induced skin cancer

(8) The postulation that, since heat is a known mutagen and there is a strong correlation between mutagenesis and carcinogenesis, under certain conditions of relatively high-intensity exposure, RF radiation that causes significant tissue heating could theoretically induce cancer

(9) The lack of well designed human or animal studies that have sufficient exposure data and are statistically adequate to provide credible data that would support a reliable conclusion.

Reviewed in depth herein are four published reports that have received extensive publicity, including (1) the Prausnitz and Süsskind (1962) report of leukemogenesis in mice chronically irradiated with microwaves, (2) the "North Karelia Connection" suggested by Zaret (1976), (3) the irradiation of U.S. Government employees stationed at the U.S. Embassy in Moscow (Lilienfeld et al. 1978), and (4) the health status of U.S. Navy personnel exposed to radar during the Korean War (Robinette et al. 1980). Brodeur (1977) gives anecdotal accounts of increased incidence of cancer in several groups of defense contract personnel working in RF-radiation research and development, but no reliable reports on these incidents have appeared in the scientific or medical literature. Since the cutoff date for general literature review, two letters to the editor have appeared in the New England Journal of Medicine suggesting an association of polycythemia vera with occupational microwave exposure (Friedman 1981) and leukemia with occupational exposure to a variety of electric and magnetic fields (Milham 1982). Neither of these letters would meet the criteria established for this review but should lead to more elaborate studies to resolve the questions raised.

5.9.3 Prausnitz and Süsskind Study

In 1962, Prausnitz and Süsskind published reports on an experiment conducted to determine the pathological and life-shortening effects of chronic microwave exposure of mice. In 200 male Swiss mice irradiated with 9270 MHz (PW) at an average power density of 100 mW/cm^2 for 4.5 min daily, an average body temperature increase of 3.3 °C was produced. Exposures were conducted 5 days/week for 59 weeks, and survival, body mass, blood parameters, and certain postmortem pathological findings were compared with those of a concurrently sham-irradiated group of 100 animals. Animals were sacrificed at 7, 17, and 19 months after the beginning of irradiation. In addition, 23 percent of the animals were lost to the study by spontaneous death and autolysis prior to necropsy. The remaining 100 animals (40 controls, 60 irradiates) formed a "longevity" study group. One of the findings reported in this group was "cancer of the white cells," defined as monocytic or lymphocytic leucosis, or lymphatic or myeloid leukemia. Leucosis was defined as a noncirculating neoplasm of the white cells, whereas leukemia was defined as a circulating leucosis. Data were grouped and reported as "leucosis." Although the liver and spleen were removed for examination at necropsy, they were not considered in determining lymphoid infiltration, even though these organs are usually involved in this kind of reaction. Data describing the differential composition of the blood cell types are not given. A summary of the fate of the 200 irradiates and 100 controls is shown in Table 5-23.

The results as reported are confusing. The authors performed a third sacrifice series at 19 months to resolve a perceived contradiction in the "leucosis" findings from the first and second sacrifice series. Yet, had they used even a crude 2 x 2 contingency table analysis to test the prevalence of leucosis in the control and irradiated animals sacrificed in the second series, they would have arrived at a χ^2 of only 1.49 (uncorrected for continuity) with one degree of freedom ($P > 0.20$). Thus, the prevalence of leucosis in irradiated animals was not significantly different from that in the control animals for any of the "sacrifice" groups.

While leucosis in the "longevity" series is highly significant ($P < 0.005$, $\chi^2 > 8.0$), these data are severely compromised by (1) the marked loss of animals that would have fallen in this group due to autolysis, (2) the differential loss of control animals due to infection, and (3) the premature sacrifice of all remaining animals to resolve a nonexistent paradox. Comparing data from two groups of animals that selected themselves (by dying prior to 19 months and being found in time for necropsy) is not an acceptable statistical analysis of experimental data. An acceptable method would be to compare the prevalence rates of leucosis in the controls and irradiates in combined groups that include all the animals at risk in the original longevity group (longevity and third sacrifice series). If this is done, the following results are obtained:

Group	With Leucosis	Without Leucosis	Total
Control	8 (a)	51 (b)	59 (a+b)
Irradiated	33 (c)	94 (d)	127 (c+d)
Total	41 (a+c)	145 (b+d)	186 (n)

To test whether the leucosis rates are different in controls and irradiates, the following statistic may be used:

$$S = n(ad - bc)^2/[(a+b)\ (c+d)\ (a+c)\ (b+d)]$$

If the animals comprising the table represent a random sample from a larger population, S approximately follows a χ^2 distribution with one degree of freedom. Upon substitution, the value of 3.72 is obtained. Since $\chi^2 > 3.62$ ($P \triangleq 0.06$), the rates would not be declared different at the 5 percent significance level. Furthermore, if a continuity correction were used in computating this statistic, the resultant $\chi^2 = 2.93$, which is significant only at the 9 percent level.

There are now better statistical methods available to analyze survival data (Peto *et al*. 1976, 1977), but they require detailed documentation of the fate of each animal during the course of the experiment. Given (a) the loss of histopathological data on animals because of autolysis and infection, (b) the further complication that different pathologists were used for different sacrifice series, and (c) the absence of historical data on the incidence of leucosis in the mouse strain used, any attempt to apply these methods retroactively would not be beneficial.

In summary, because of the previously described problems with the biological protocol, the lack of sound statistical methodology in experimental design and data analyses, and the questionable significance of what was reported, the study by Prausnitz and Süsskind is of limited value in defining the pathological effects of chronic whole-body microwave radiation. As noted previously, the data on survival times are of considerable interest due to similar findings by Spalding _et al_. (1971) and Preskorn _et al_. (1978).

5.9.4 North Karelia Connection

In 1971, the Finnish government, in conjunction with the World Health Organization, began a program known as the "North Karelia Project" (Puska _et al_. 1978). Finland has one of the highest rates of mortality from cardiovascular disease (CVD) in the world. Within the country, the eastern provinces had higher rates of CVD than those in the west. North Karelia, an eastern province that borders the Soviet Union, was identified in the 1950's as having a particularly high incidence of CVD. The objectives of the project were to decrease CVD morbidity and mortality by identifying the causative factors, devising means for primary prevention, and strengthening treatment and secondary prevention. Cigarette smoking, elevated blood pressure, and serum cholesterol levels were postulated as three major risk factors. The proximity of North Karelia to the Soviet border prompted an American physician, Dr. Milton Zaret, to speculate that RF radiation from Soviet communications or radar might be contributing to the incidence of CVD. In a presentation at the symposium Biologic Effects and Health Hazards of Microwave Radiation (Warsaw, October 15 to 18, 1973), he suggested that microwave radiation from the Soviet Union might be a factor. His remarks were later withdrawn and do not appear in the record of the Symposium. However, he restated this hypothesis in a published article (Zaret 1976), in which he additionally stated, without data or reference, that "a new finding, an increased incidence of cancer, also appears to be emerging in North Karelia." The major thrust of the article was directed to the possibility of exploiting the North Karelia Project to investigate the role of RF radiation in the evolution of CVD. He also noted that the potential role of RF radiation in carcinogenesis should be studied.

In their literature review on carcinogenic properties of microwave and RF radiation, Dwyer and Leeper (1978) misinterpreted the 1976 Zaret article. They editorially transformed the North Karelia Project into an epidemiological project designed to test the hypothesis that RF radiation caused or contributed to heart attacks or cancer.

The Finnish Project (1972 to 1977) caused significant changes in diet and lifestyle, which correlated with a significant reduction in CVD mortality. Further, information provided by the Finnish Institute of Radiation Protection (K. Jokela, personal communication to M. Hattunen, Scientific Counselor of Embassy of Finland, 2133 Wisconsin Avenue, N.W., Washington, D.C. 20007, November 22, 1978) specifically denies the existence of an abnormal cancer incidence in eastern Finland and knowledge of any possible linkage to microwave fields.

5.9.5 Moscow Embassy Study

The long-term microwave irradiation of the American Embassy buildings in Moscow was highly publicized in 1976. This led to a comprehensive study of the morbidity and mortality of the Moscow Embassy employees and dependents as compared with employees and dependents of U.S embassies in other Eastern European locations (Lilienfeld *et al*. 1978).

The Moscow group experienced less overall mortality for all causes of death than did the comparison group. However, the death rate in females from malignant neoplasms was slightly, but not significantly, higher than expected in the Moscow group; and the incidence of malignant neoplasms, other than of the skin, was significantly higher in the Moscow female group. In both cases, the numbers were very small. In the former case, there were 7 different cancer sites involved in 8 cases, which, according to the authors, virtually eliminates a single causal factor; in the latter case, there were 10 cases involving 7 different sites, and, when exposure to microwaves was considered, it was found that the death rate was highest for those who had the least exposure to microwaves.

5.9.6 U.S. Navy Study

A study of the effects of occupational exposure to radar during the Korean War on U.S. Navy enlisted personnel was recently published (Robinette *et al*. 1980). Approximately 20,000 men whose occupations possibly involved relatively more frequent exposures to higher intensity fields were compared with 20,000 men in other occupational classifications. One of the end points evaluated was the effect of exposure from 1950 to 1954 on the relative incidence of cancer during 1950 to 1976. No statistically significant differences between the two groups were evident for malignant neoplasms as a cause of death from 1950 to 1974, or as a cause of hospitalization in Navy or VA hospitals. Within the high exposure group, subgroups were created, depending on Hazard Number. The Hazard Numbers were measures of potential individual exposures, dependent upon the type and power rating of the radar and upon the ship and the time spent in service on the ship. Hazard Number categories were 0, 1 to 5000, and $>$ 5001. In considering the causes of death within the highest exposure group, there are significantly more malignant neoplasms of the respiratory tract in the subgroup with Hazard Number $>$ 5001 than in the subgroup with the Hazard Number $<$ 5000. A significant trend for increased death from all diseases in the $>$ 5001 subgroup was also noted. However, information relevant to respiratory neoplasms such as smoking histories was not available because the study was an analysis of cause of death from death certificate data. Also, in a study where so many statistical comparisons are done using a $P = 0.05$ criterion, one or two positive findings would be expected by chance.

5.9.7 Unresolved Questions

Because few RF-radiation studies in man or animals have employed life span or cancer as end points, and none has had sufficient statistical power and adequate quality control to place an upper limit of risk at less than two times control incidences, the questions of microwave carcinogenesis or life shortening are still open. Conversely, none of the complete reports in the literature presents a convincing case for the existence of a significantly increased risk of cancer or life shortening in exposed populations. A critical issue is the difficulty of developing exposure data or information in human population studies.

The interaction of RF radiation with other moieties (such as ionizing radiation) in the induction, prevention, or treatment of cancer has not been fully characterized. Microwave-induced hyperthermia has been demonstrated to increase the effectiveness of x-ray treatment of various cancers. In nontherapeutic situations, however, both inhibition and enhancement of tumor development in microwave-irradiated mice have been reported.

In their paper, discussed in the section on longevity (§ 5.9.1, Life Span), Preskorn _et al_. (1978) found that the development of tumors following injection of sarcoma cells into 16-day-old CFW mice was significantly delayed if the mice had been exposed to 2450-MHz microwaves _in utero_ on day 11, 12, 13, and 14 of gestation (20 min/day, SAR = 35 W/kg). There was no difference, however, in the ultimate number of tumors.

Conversely, Szmigielski _et al_. (1980) found that repeated exposure to 2450-MHz microwaves 5 or 15 mW/cm^2 (SAR 2 to 3 or 6 to 8 W/kg), 2 h/day, 6 days/week for up to 10 months significantly accelerated the appearance of spontaneous breast tumors in C_3H/HeA mice, and the appearance of skin cancer in BALB/c mice treated with 3,4-benzopyrene during or after the microwave exposure. It is noted that chronic stress due to deliberate overcrowding produced essentially the same effect as the 5 mW/cm^2 exposure. In both experiments, 15 mW/cm^2 produced greater acceleration in tumor production than did 5 mW/cm^2 or overcrowding. Workers in this field have only begun to discover the effects of RF-radiation on animals under different immunologic and hormonal equilibrium levels, e.g. animals subjected to prolonged stress.

5.10 HUMAN STUDIES

Doreen Hill

The general approach used in this document for the evaluation of the health effects literature is stated in the Introduction. Rigorous criteria were established and applied to the reports of experimental results in order to establish what is believed to be a credible data base. It is, however, difficult to apply these selection and review criteria uncompromisingly to the human studies or epidemiological literature, largely because the research method is population-based and observational rather than experimental. The papers included here were selected because they were judged to present relatively more information on exposure parameters and/or more rigorous or analytical study designs. The amount of detail in reporting and the degree of specification of study methods and procedures (use of controls, statistics, control of confounding variables, and so forth) were considered important. Case reports are not included.

5.10.1 Occupational Surveys/Clinical Studies

The majority of reports in the literature concern people occupationally exposed in military or industrial settings. A wide variety of conditions, symptoms, and clinical measurements are usually evaluated. The health conditions investigated usually are pre- or subclinical instead of overt or diagnosed disease. Studies of this type that focused on single rather than multiple end points are described later.

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It is in occupational surveys and industrial health surveillance programs that the potential for neurological and behavioral changes has been investigated. The Soviet and Eastern European literature frequently describes a collection of symptoms reported to occur in personnel industrially exposed to microwaves. These collective symptoms, which have been variously called the "neurasthenic syndrome," the "chronic overexposure syndrome," or "microwave sickness," are based on subjective complaints that include headaches, sleep disturbances, weakness, decrease of sexual activity (lessened libido), impotence, pains in the chest, and general poorly defined feelings of non-well-being (Baranski and Czerski 1976, p. 157). Also described are a set of labile functional cardiovascular changes including bradycardia (or occasional tachycardia), arterial hypertension (or hypotension), and changes in cardiac conduction, and this form of neurocirculatory asthenia is also attributed to nervous system influence (Silverman 1980).

Barron et al. (1955) presented results of a study conducted to evaluate changes in various physical and functional characteristics of radar personnel employed by an airframe manufacturer. A total of 226 exposed workers were initially included in the medical surveillance program. The radar workers were characterized by their duration of exposure as seen in Table 5-24. Controls totaling 88 subjects, stated to have had no industrial radar exposure, were also examined. Methods of selection of cases or controls were not specified. The age distribution of all subjects ranged from 20 to more than 50 years, with the majority under 40 years of age. The controls were, however, substantially older, as can be seen in Table 5-25.

TABLE 5-24. DISTRIBUTION OF YEARS OF EXPOSURE FOR 226 RADAR WORKERS*

Years of Exposure	No. of Workers	Percent of 226
0 to 2	106	47
2 to 5	83	37
5 to 13	37	16

*Data from Barron _et_ _al_. 1955.

TABLE 5-25. AGE DISTRIBUTION OF 226 MICROWAVE WORKERS AND 88 CONTROLS*

	Radar		Controls	
Age	% of 226	Cumulative %	% of 88	Cumulative %
20 to 29	34	34	14	14
30 to 39	49	83	40	54
40 to 49	13	96	27	81
50+	4	100	19	100

*Data from Barron _et_ _al_. 1955.

A decrease in polymorphonuclear cells was reported in 25 percent of the radar workers vs. 12 percent of the controls. An increase in monocytes and eosinophils was also observed for the exposed group, but in a later report (Barron and Baraff 1958) these effects were attributed to a technical error. Platelet counts and urinalyses were similar in the two groups. Ophthalmological examinations revealed ocular anomalies of several diverse types among

12 exposed persons vs. 1 case in the control group. The medical surveillance program was extended to permit periodic reexaminations (Barron and Baraff 1958). No significant changes in health status were noted.

The radar bands of exposure include S-band (2880 MHz) and X-band (9375 MHz). Exposure times and power densities for individuals could not be developed, but zones at various distances from the antenna were specified and used to estimate three ranges of power densities. The minimal average power density in Zone A was 13.1 mW/cm^2. Zone B ranged from 3.9 to 13.1 mW/cm^2. Zone C was <3.9 mW/cm^2. The authors stated that because of the relatively low power densities, personnel working in Zone C were eliminated from the study. The majority of personnel worked with or around APS-45 and AN/APS-20-B and -E radars. By establishing these zones of potential exposure, steps were taken to limit entry of personnel to Zone A. Zone B was judged to be safe for occasional but not constant exposure. As a result, most subjects continuing in or added to the examination program are believed to have had only incidental exposures to power densities less than 13.1 mW/cm^2.

The strengths of this study are the attempts to estimate potential exposures and to periodically reexamine the workers. But, there are also some major problems with study methods and analyses. For example, there are disproportionate numbers of exposed vs. control subjects as well as questionable comparability because of age differences (Table 5-25). None of the observed results were tested statistically.

Czerski, Siekierzynski, and co-workers in Poland evaluated 841 men occupationally exposed to pulse-modulated microwave radiation (Czerski et al. 1974; Siekierzynski et al. 1974a, 1974b). The radiation frequencies were not explicitly stated, but one can infer from the references to pulse-modulation and radio-location that the working environment dealt with radar frequencies. The age distribution of the men ranged from 20 to 45 years. The men had worked varied periods of time, with some employed over 10 years. An unexposed control population comparable in general working conditions and socio-economic status could not be established; therefore, the study group was subdivided into two groups on the basis of level of microwave exposure. One group consisted of 507 men exposed to mean power densities greater than 0.2 mW/cm^2, with short-term exposures estimated to reach 6 mW/cm^2. The other group was 334 men exposed to mean power density levels less than 0.2 mW/cm^2.

The health end points evaluated covered three major categories, e.g., neurotic syndrome, digestive tract functional disturbances, and cardio-circulatory disturbances with abnormal electrocardiogram (ECG) findings. According to Polish occupational exposure criteria, these conditions are considered contraindications for work in a microwave environment. The neurotic syndrome was defined by a variety of symptoms such as fatigue, headaches, sleep disturbances, and difficulties in memorizing and concentrating. Psychologic examinations were given. Comparisons were made between and within exposure groups according to age and duration of occupational exposure. The two groups were found to be similar with respect to the distribution of these symptoms and conditions. There was no dependence on the duration of exposure.

In 1979, Djordjevic et al. reported on medical evaluations of radar workers, aged 25 to 40 years, with a work history of 5 to 10 years. Specific frequencies of exposure were not cited but were stated to be within the whole range used in radar operations. Evaluation of the working environment was undertaken, including power density measurements. While the environmental analyses are not given in the paper, it was concluded that the workers were exposed to pulsed microwaves within a wide range of intensities but generally at levels less than 5 mW/cm^2. The lower limit of this exposure may have been 1 mW/cm^2, but it is not clear from the discussion whether this estimate refers to the workers included in this study or to radar station personnel in general. The control group consisted of 220 persons reported to be similar in age, working environment, and socioeconomic status. The controls did not have work experience with microwave sources. Selection criteria or further descriptive information was not given for either the cases or controls.

Ten major end points or diagnoses were covered in the clinical evaluation, including ophthalmologic examinations. These were conducted by clinical specialists following the same scheme for classification of abnormalities. The two groups did not differ with respect to the 10 factors. The type of procedure was not reported. The groups also did not differ statistically in terms of electrocardiogram results or on multiple biochemical and hematologic indicators. Radar workers did demonstrate more subjective complaints, including headache, fatigue, irritability, sleep disturbance, inhibition of sexual activity, and impairment of memory. Based on their survey of working conditions, the authors attribute the latter result to specific problems such as lighting or poor ventilation in the environment of the radar workers. If true, it appears that either the subject and control groups were not as comparable with respect to working environment as originally stated, or some other factor(s) is (are) operating to produce more subjective complaints. One possibility is a selective or reporting bias on the part of the radar workers, e.g., enhanced awareness of the possible "microwave sickness" syndrome. Some other environmental factor may have been present that may not be measurable in the type of environmental survey conducted or detectable through these clinical evaluations but microwave exposure cannot be clearly excluded.

5.10.2 Mortality Studies

Lilienfeld and associates (1978) completed a broad survey of the mortality and morbidity experience of Foreign Service employees and their dependents to assess the potential health consequences of microwave irradiation of the American Embassy in Moscow. Foreign Service employees and those from other agencies who had served in the Moscow Embassy during 1953 to 1976 were compared with employees at eight other embassies or consulates in Eastern Europe over the same time period.

The microwave irradiation of the Moscow Embassy was first detected in 1953 and subsequently varied in intensity, direction, and frequency over time. The frequencies ranged from 0.6 to 9.5 GHz (United States Senate, Committee on Commerce, Science, and Transportation 1979; Pollock 1979). The measured average power densities over time are given in Table 5-26.

TABLE 5-26. MICROWAVE EXPOSURE LEVELS AT THE U.S. EMBASSY IN MOSCOW

Time Period	Exposed Area of Chancery	Power Density and Exposure Duration
1953 to May 1975	West Facade	Max of 5 $\mu W/cm^2$ 9 h/day
June 1975 to Feb. 1976	South and East Facade	18 $\mu W/cm^2$ 18 h/day
Since Feb. 7, 1976	South and East Facade	Fractions of a $\mu W/cm^2$ 18 h/day

*Data from Lilienfeld _et_ _al_. 1978.

Extensive efforts were launched to identify and trace the populations. Information on illnesses, conditions, or symptoms were sought from two major sources: (1) employment medical records, which were fairly extensive, given examination requirements for foreign duty and (2) a self-administered health history questionnaire. Questionnaire responses were validated for a stratified sample by review of hospital, physician, and clinic records. Death certificates were also sought, although other sources also were used to ascertain mortality status.

Standardized mortality ratios for various subgroups were developed for each cause of death, were standardized for age and calendar period, and were specific for sex. Similar procedures were applied to develop summary indices of morbidity.

A total of 4388 employees and 8283 dependents was studied. More than 1800 with 3000 dependents were employed at the Moscow Embassy and 2500 with more than 5000 dependents worked at the comparison posts. Ninety-five percent of the employees were traced. Receipt of completed questionnaires was less successful, with an overall response rate of 52 percent for State Department personnel.

Hundreds of comparisons between the Moscow and control posts were made from information in the medical records. Various health problems were generally similar with two exceptions. Moscow employees had a threefold greater risk of acquiring protozoal infections than comparison-post employees. In general, both sexes in the Moscow group had somewhat higher frequencies of most of the common kinds of health conditions reported. The authors stated, "However, these most common conditions represented a very heterogeneous collection and it is difficult to conclude that they could have been related to exposure to microwave radiation since no consistent pattern of increased frequency in the exposed group could be found."

Some excesses were reported by Moscow employees in the health history questionnaire. Both sexes reported more eye problems due to correctable refractive errors. More psoriasis was reported by men and anemia by women. The Moscow employees, especially males, reported more symptoms such as irritability, depression, difficulties in concentration, and loss of memory. It is possible, however, that a bias due to awareness of potential adverse effects is operating, since the strongest differences were present in the subgroup with the least exposure.

The observed mortality was less in both male and female employees than expected, based on U.S. mortality rates; the male employees had more favorable experience than female employees. In both sexes, cancer was the predominant cause of death. The Moscow and comparison groups did not differ appreciably in overall and specific mortality. The authors noted, however, that the population was relatively young, and it may be too early to detect long-term mortality effects.

The authors concluded that no convincing evidence was discovered to implicate microwaves in the development of adverse health effects at the time of the analysis. But they also carefully discussed the limitations inherent in the study. These included uncertainties associated with the reconstruction of the employee populations and dependents, difficulties of obtaining death certificates, the low percentage of responses for the questionnaire, and the statistical power of the study. The limitation most critical for consideration in a document such as this relates to ascertainment of exposure. Problems relative to individual mobility within the embassy and variation of field intensities within the building are present in this study as in any other. No records were available on where employees lived or worked, so one had to rely on questionnaire responses to estimate an individual's potential for exposure. The highest exposure levels (18 $\mu W/cm^2$) were recorded for only 6 months in 1975-76, thus the group exposed to the most intense fields had the shortest cumulative time of exposure and of observation in the study.

Robinette and Silverman (1977) and Robinette _et al_. (1980) examined mortality and morbidity among U.S. naval personnel occupationally exposed to radar. Records of service technical schools were used to select subjects for the study. Exposure categorizations were made on the basis of occupational specialty. The exposure group (probably highly exposed) consisted of technicians involved in repair and maintenance of radar equipment. The controls (probably minimally exposed) were involved in the operation of radar or radio equipment. It was estimated from shipboard monitoring that radiomen and radar operators (in the low-exposure group) were generally exposed at less than 1 mW/cm^2, while gunfire control and electronics technicians (in the high exposure group) were exposed to higher levels during their duties. Over 40,000 veterans were included in the study, with about equal numbers in these two major exposure classifications. In conjunction with naval personnel, an effort was also undertaken to develop an index of potential exposure, termed Hazard Number, for a limited portion of the population. This number was based on the duty months multiplied by the sum of the power ratings (equipment output power) of gunfire-control radars (ship) or search radars (aircraft) where technicians were assigned.

Medical information was obtained through Navy and Veterans Administration records. Records were searched for information on four major end points: (1) mortality; (2) morbidity via in-service hospitalizations; (3) morbidity via VA hospitalizations; and (4) disability compensation.

Mortality was ascertained through the VA beneficiary system. Strokes, cancers of the digestive tract and respiratory system, and leukemias were elevated for the high exposure group, but none of the increases was statistically significant. The authors note that the differences in mortality from malignant neoplasms of the lymphatic and hematopoietic system are not statistically significant. As seen in Table 5-27, comparisons were also made within the high exposure group across Hazard Number categories. In this case, only two comparisons were statistically significant: (1) the difference in

TABLE 5-27. NUMBER OF DEATHS FROM DISEASE AND MORTALITY RATIOS[a] BY HAZARD NUMBER: U.S. ENLISTED NAVAL PERSONNEL EXPOSED TO MICROWAVE RADIATION DURING THE KOREAN WAR PERIOD[b]

			Number of Deaths			
			High Exposure, by Hazard No.			
Cause of Death	International Classification of Diseases (8th Rev.)	Low Exposure	Total	0	1-5000	5000+
All diseases	000-796	325 (1.04)	309 (0.96)	63 (0.82)	160 (0.91)	86 (1.23)
Malignant neoplasms	140-209	87 (0.96)	96 (1.04)	22 (0.99)	45 (0.90)	29 (1.44)
Digestive organs	150-159	14 (0.85)	20 (1.14)	6 (1.49)	11 (1.14)	3 (0.78)
Respiratory tract	160-163	16 (0.85)	24 (1.14)	4 (0.82)	10 (0.86)	10 (2.20)
Lymphatic and hematopoietic system	200-209	20 (0.83)	26 (1.18)	6 (1.09)	12 (1.04)	8 (1.64)
Other malignant neoplasms	Residue	37 (1.19)	26 (0.82)	6 (0.78)	12 (0.70)	8 (1.17)
Diseases of circulatory system	390-458	167 (1.07)	150 (0.93)	36 (0.94)	73 (0.83)	41 (1.17)
Other diseases	Residue	71 (1.08)	63 (0.92)	5 (0.30)	42 (1.13)	16 (1.08)

[a] Mortality ratio (in parentheses) standardized for year of birth; the combined experience of the low and high exposure groups is taken as the standard.

[b] Data from Robinette _et_ _al_. 1980.

respiratory tract cancer between those with a Hazard Number less than 5000 vs. more than 5000 and (2) the test for trend for all diseases combined. However, information relevant to respiratory neoplasms such as smoking histories was not available because the study was an analysis of cause of death from death certificate data. Differential health risks with respect to hospitalized illness around the period of exposure were not apparent. Subsequent VA hospitalizations and disability awards provided incomplete information.

Since the study focused largely on the use of automated VA record systems, it was not possible to determine non-Navy or non-VA hospitalizations, nonhospitalized conditions, reproductive histories, or subsequent employment histories. Actual individual exposure could not be reconstructed retrospectively, thus the information represents the potential exposure of the men.

5.10.3 Ocular Effects

Many surveys on ocular effects have been conducted. The potential of RF radiation to induce cataracts and the production of lens defects and opacities have been cited in both American and foreign literatures. Ocular effects have, in fact, been the major end point of study in U.S. research, primarily in military populations. For this health end point more than others, much attention has been devoted to careful, detailed clinical examinations and to use of standard procedures or protocols. Population selection criteria, however, is not well elaborated; therefore, the possibility of selection bias cannot be excluded for most of these surveys. Ocular studies have largely taken the form of cross-sectional clinical surveys in actively working populations and, as such, have focused on minor lens changes. Longitudinal studies of populations with known exposure, with followup of either a prospective or retrospective nature, are nonexistent despite the identification of potential cohorts from the cross-sectional surveys. The research to date has not yet fully examined the question of whether lens changes, if observed, lead to overt clinical eye disease or conditions, e.g., the functional and clinical significance of minor lens changes in general and over time. Thus, while it appears reasonable that RF radiation at high levels could influence cataract-ogenesis, it cannot be confirmed without more rigorous followup studies in already identified exposed populations. This would be a reasonable line of future research if such epidemiological studies are feasible.

Utilizing Veterans Administration hospital records and military personnel records, Cleary _et_ _al_. (1965) conducted a case-control study to examine cataract formation among Army and Air Force veterans. This is the only case-control study focused on clinically diagnosed cataracts. Cases were defined as white males born after 1910 who were treated for cataracts between 1950 and 1962, based on diagnoses given in VA hospital records. Controls were drawn from the same sources by selecting men with adjacent hospital register numbers; therefore, the control group had random diagnoses made in the same hospitals at the same time the cataract cases were diagnosed, and the controls were also born after 1910. Military occupational specialties, as abstracted from service records, were used to denote radar or nonradar workers. Job classification was then used as an indicator of potential exposure. The distribution of cases and controls according to radar exposure is seen in Table 5-28. The frequency of microwave exposure as denoted by radar-work history was similar between cases and controls; the odds ratio was less than one (0.67) and was not statistically significant. The distribution over all age groups is seen in Table 5-29. Excess risk was noted for Air Force veterans, but the numbers were small. Only 40 radar workers were found in over 5000 cases and controls.

TABLE 5-28. CLASSIFICATION BY MILITARY OCCUPATION OF WORLD WAR II AND KOREAN WAR VETERANS WITH AND WITHOUT CATARACTS, BASED ON DISCHARGES FROM VA HOSPITALS*

	Veterans' Cataract Status		
Occupation	Yes	No	Total
Radar Workers	19	21	40
Nonradar Workers	2625	1935	4560
TOTAL	2644	1956	4600

$$\text{Odds Ratio} = \text{OR} = \frac{(19)\ (1935)}{(21)\ (2625)} = 0.67$$

*Data are from Cleary *et al*. 1965.

Cleary and Pasternack (1966) examined and scored subclinical or minor lens changes in 736 microwave workers and 559 controls. A relative exposure index or score was developed by weighing various parameters such as power output and distance from the microwave generating source. The work environment in terms of microwave parameters was not specified. Utilizing regression techniques, radar workers were found to have more lens changes than controls, and the number of defects was correlated with duration of exposure and exposure score among the workers. The authors suggested that the subclinical changes may indicate accelerated aging of lens tissues.

TABLE 5-29. ESTIMATED RELATIVE RISK OF CATARACTS AMONG ARMY AND AIR FORCE VETERANS*

Cataracts		Radar Workers	Nonradar Workers	Odds Ratio	χ^2
Total	Yes	19	2625	0.67	1.26 NS
	No	21	1935		
20-39	Yes	3	418	0.94	0.08 NS
	No	4	522		
40-49	Yes	7	1517	0.39	3.39 NS
	No	13	1101		
50-59	Yes	9	699	1.02	0.09 NS
	No	4	316		

*Data are from Cleary *et* *al*. 1965.

Majewska (1968) studied the eyes of 200 Polish workers employed from 6 months to 12 years at installations with microwave-generating equipment that operated from 600 MHz to 10.7 GHz (2.8 to 50 cm). Although cited as "high intensity" by the author, intensity levels were not specified. Two hundred comparably aged unexposed controls were also examined. No methods of subject selection were reported, nor was the sex of the participants reported. After dilation of the subjects' pupils, lenses were examined with an ophthalmoscope and a slit lamp. It was not stated whether procedures ("blinding") were applied to mask the group assignment of the subjects for the examiners. Lens changes were noted in 168 of the subjects vs. 148 controls. This difference was calculated as statistically significant. The result was presented as a summary measure over all ages; age-specific differences were not presented. The authors stated that the controls were age-matched.

In the same study, the effects of longer-term exposure were evaluated by comparing 100 controls with 102 employees, drawn from the original group, who had worked with high-frequency-electromagnetic-wave generators for more than 4 years. Subjects were graded on a five-point scale for degree of lens opacity. The mean grade of opacities in the exposed group was greater than in controls in each 5-year age-group interval for ages ranging from 20 to 50 years. Among microwave workers, the mean grade of lens changes, uncontrolled for age, also showed an increase with length of employment. Although this part of the study was stated to be focused on employees with four or more years of work experience, the data on lens scores and duration of employment list results for persons with less than four years of employment. This evaluation also suffers from a lack of quantitative measures of exposure.

In 1972, Appleton and McCrossan reported a clinical survey conducted among 226 military personnel stationed at Fort Monmouth, New Jersey. Microwave-exposed workers were defined as those who worked with Signal Corps electronic communication, detection, guidance, and weather equipment. Controls did not report such a work history. Likely intensities or frequencies were not specified. There were 135 controls and 91 exposed personnel. Personnel were drawn from the post's Occupational Vision Program, but sampling or selection procedures were not documented. Ophthalmologists based diagnoses on slit-lamp examination of dilated pupils. The presence or absence of opacities, vacuoles, and posterior subcapsular iridescence was noted. The examination results were similar in the two groups over all age groupings, although no statistical tests were applied.

The survey was later extended to six other installations with results reported by Appleton in 1973. The exposure of military personnel was classified as "likely" vs. "unlikely." The latter group served as controls. Blind procedures were utilized for the examining ophthalmologists; that is, they were not aware of the exposure classification of subjects. The same team of examiners performed all tests, except at one location, in an attempt to minimize inter-observer variation. The same three end points used in the 1972 study were also used in the 1973 study. Older age groups demonstrated a trend of greater opacities among exposed personnel, but, since the numbers in some age groups were small, the validity of this result is questionable.

Odland (1973) reported results of a survey of ocular anomalies in personnel from eight military installations. The population consisted of 377 exposed individuals and 320 controls. Exposure conditions were not specified. Exposed personnel were defined as individuals whose primary duties involved the operation or maintenance of radar equipment. The selection criterion for controls was duty that did not permit actual or potential exposure to radar. The actual work assignments of control persons were not stated. Medical histories were taken, and ophthalmic examinations were performed in a double-blind manner. The occurrence of lens anomalies was similar in the two groups; however, the frequency of anomalies between control and exposed groups was different for individuals who had a family history of diabetes, nontraumatic cataract, glaucoma, or defective vision. Lens changes were noted in 29 percent of the exposed individuals with such a history vs. 17 percent in the controls with a family history of eye problems. No statistical tests were applied to any of the reported frequency distributions.

Shacklett et al. (1975) reported eye examinations of 817 military and civilian personnel. There were 477 persons with a history of microwave exposure and 340 controls without exposure drawn from eight Air Force bases between November 1971 and December 1974. The authors stated that detailed work histories were recorded (including time with different types of equipment), but information on typical exposure settings is not given Local unit commanders selected the subjects by using criteria established by the examining team. Standard diagnostic criteria were established. The same ophthalmologists performed all examinations and were not aware whether a subject was considered as exposed or a control. No differences were noted between the two groups in the frequency of opacities, vacuoles, and posterior subcapsular iridescence. Differences in results were not statistically significant, but the type of test was not stated. An age-dependent increase in lens changes was noted in both groups.

The study by Siekierzynski et al. (1974b) discussed earlier also compared lens opacities in the two exposure groups (less than 0.2 mW/cm^2 and 0.2 to 6 mW/cm^2). Ophthalmologic examinations were performed. Lens translucency was assessed with a slit lamp after pupil dilatation and according to criteria established for five grades. No differences were reported between the exposure groups nor within the groups for duration of exposure.

5.10.4 Reproductive Effects

In 1965, Sigler et al. reported a history of occupational exposure to radar and more military service among fathers of children with Down's Syndrome.

The association with radar exposure was an ancillary observation; this study was specifically directed toward examination of the relationship between ionizing radiation exposure and Down's Syndrome. A case-control approach was used, and 288 children born with Down's Syndrome in Baltimore between January 1946 and October 1962 were identified for inclusion in the study. Controls were selected by matching each case of Down's Syndrome with another normal birth for (1) hospital of birth, (2) sex, (3) date of birth, and (4) maternal age at birth of child. Of the original 288, 216 matched pairs were available for final analysis. Eliminations occurred for various reasons such as non-cooperation or equivocal diagnoses. Occupational histories and other data were obtained by interview of the parents. The fathers of the children with Down's Syndrome had more military service experience than control fathers, but the difference was not statistically significant. A greater history of radar exposure, as radar technicians or operators, was reported by case fathers. This difference was statistically significant. It should be noted that radar operators are not necessarily "exposed," since the place of operation may be away from the power-generating equipment or the microwave source.

Cohen _et_ _al_. (1977) extended the study. The case series was expanded to include 128 additional verified cases and their matched pairs born through 1968. To serve as an independent replication, essentially the same procedures were applied along with the following expansions: (1) more extensive questions on microwave/radar exposure and military service, (2) validation of exposure histories by searching armed service records, and (3) chromosomal studies. The previously noted differences disappeared in the extended analysis as seen in Table 5-30. Results of the cytogenetic analyses are not yet available.

TABLE 5-30. PATERNAL RADAR EXPOSURE BEFORE CONCEPTION OF INDEX CHILD (FROM INTERVIEW AND/OR NAS)[a]

Case Series[b]		Down's Cases No.	Down's Cases %	Controls No.	Controls %
1. Current	Exposed	20	15.7	27	21.3
	Exposure Known	127	100.0	127	100.1
2. Original	Exposed	36	18.6	30	15.2
	Exposure Known	194	100.1	198	100.0
3. Combined	Exposed	56	17.4	57	17.5
	Exposure Known	321	99.9	325	100.0

[a] Data are from Cohen *et al*. 1977.

[b] 1: 128 pairs; 2: 216 pairs; 3: 344 total pairs.

The authors stated that although the extended study did not confirm excess radar exposure among Down's case fathers, the possible relationship of such exposure to increased risk of Down's offspring cannot completely be ruled out. They added further that the most challenging aspect of the investigation was the definition of radar "exposure." In discussing explanations for lack of confirmation of a radar exposure factor (if one does in fact exist) the authors offer several possibilities. As mentioned above, inaccurate exposure estimates could distort results. The role of maternal factors in Down's Syndrome is so important that paternal factors could be masked. It was also suggested that the most severely impacted males with the highest risk of abnormal offspring also experienced germinal tissue damage, eliminating them from reproductive experience or ascertainment through live birth cases. It was further suggested that a prospective approach might, then, prove more fruitful. Although not discussed by the authors, radar equipment and military occupational specialties could have changed over time in such a way as to lower risk. It has also been suggested that since microwave-generating equipment, especially of an older vintage, may have emitted more ionizing radiation than modern equipment, the ionizing radiation presents the actual risk factor, with microwaves possibly operating as a co-variable.

Lancranjan _et_ _al_. (1975) studied 31 adult males with a mean age of 33 years and a mean exposure of 8 years (a range of 1 to 17 years) to electromagnetic fields that "frequently were in the range of tens to hundreds of $\mu W/cm^2$." The frequencies were defined as microwaves of wavelengths between 3 and 12 cm and frequencies between 10,000 and 3,600 MHz. No details on the RF source(s) were provided. A group of 30 men of similar mean age and no known exposure to microwaves served as a control for the analysis of spermatic fluids and hormones. Statistical analysis of the results showed no differences in urinary content of 17 keto-steroids (as an indirect measure of Leydig cell function) or total gonadotropin between the exposed and controls. Statistically significant decreases were reported for exposed personnel in the number of sperm per milliliter of semen, percent of motile sperm in the ejaculate, and the percent of normal sperm.

The goal of this study was to try to apply objective measures to assess the subjective reports of decreases in libido or of other sexual disturbances. This was accomplished, but the exposures are poorly defined, and the number of men evaluated was very small. Spermatogenesis improved in two-thirds of the subjects after cessation of exposure. The investigators felt this supported an argument for microwave influence on the observed alterations. It is interesting to note that the values obtained by the semen analyses for both exposed and control groups might be considered to be low-normal or below normal values.

Table 5-31 summarizes those studies on human beings for which SAR values could be estimated.

5.10.5 Unresolved Questions

There are some general issues surrounding the use and applicability of epidemiological research methods to study the effects of environmental agents, including radiofrequency radiation. Examples of such issues include the ability of epidemiological studies to detect low-level risks, to separate the effects of multiple causes, and to identify and control confounding factors. But, in addition, there are specific problems seen in the literature on human beings exposed to RF radiation. The reports in the literature have some important and common problems that limit interpretation and use of the data in determining population exposure levels. These problems are briefly discussed below.

5.10.5.1 Exposure Assessment--

This is perhaps the largest single problem in conducting epidemiological studies on RF radiation. It is difficult to determine the actual exposure of individuals, and even of groups, for a variety of reasons such as difficulties in developing methods of personal dosimetry for this type of radiation. There may be no continuous surveillance programs in the workplace, for example, that could yield data for use in epidemiological studies. In many cases, health studies, especially of chronic conditions, are conducted at a point in time when it is hard, if not impossible, to reconstruct exposure patterns. The study by Robinette and Silverman (1980) is a good example of attempts to deal with the difficulties of retrospective exposure assessment, e.g., two approaches (job type vs. Hazard Number) were used and an exposure gradient was obtained with the Hazard Number which simultaneously considered the RF sources and the length of service assignment. Despite these efforts, the results are still estimates of potential rather than actual exposure. On the other hand, the levels and frequencies of exposure are either not known, not estimated, or not reported in many other studies. If well-developed exposure data is not available, it is difficult to develop dose-response relationships, to interpret the significance of human health studies, and to use the data in establishing protective exposure limits.

5.10.5.2 Documentation and Methods--

Another problem in the RF radiation literature on human beings relates to documentation of methods and procedures. Degree of detail in reporting seems to be a major difference between studies done in the U.S. and those conducted in other countries. The paper "Guidelines for Documentation of Epidemiologic Studies" (Epidemiology Work Group 1981) suggests the types of topics that are useful to document when reporting an epidemiologic study, especially one used to support regulatory decisions. These major elements include background and objectives, study and comparison subjects, data collection procedures, and analysis. Few reports on human beings exposed to RF radiation adequately address these topics. It is frequently hard to tell whether certain research methods were applied or simply not reported. The selection and use of control groups is an example. The criteria for selecting controls are frequently not stated. Controls are often said to be comparable in all respects except exposure but analyses or data to support such statements may not be supplied. Also, practices such as development of standardized rates or use of procedures to control confounding variables, e.g., age adjustment, are not common in the literature. Statistical power is rarely evaluated or discussed; however, it is hard to estimate this if the underlying prevalence or incidence of the disease under study is not well known. This is especially true for some of the conditions and symptoms, e.g., functional disturbances, studied in relation to RF radiation exposure.

5.10.5.3 Health End Points: Design and Populations--

Another issue is the medical significance of any changes that may be induced by exposure to RF radiation. For example, the studies on ocular effects usually have examined a subclinical end point, e.g., lens opacities, which may not necessarily be an early marker or risk factor for cataractogenesis and visual problems (Silverman 1979). Further, the study populations have not been followed to develop incidence or longitudinal data; thus, most studies present only single measures at one point in time. Future studies should try to determine whether symptoms and subtle changes lead to any subsequent disability or disease; longitudinal data needs to be developed. A similar concern surrounds the problematic information on functional changes and nervous system effects reported in some of the Eastern European literature. Not yet substantiated, the potential for neurological or behavioral effects needs to be more thoroughly and rigorously evaluated. In addition, standardized questionnaires and more objective medical measurements need to be applied in such studies.

Most studies concern occupational groups of relatively young healthy males. It cannot be presumed that sensitivity, or lack thereof, to radiofrequency radiation exposure would be the same in the general population as in working groups. The general population is more diverse with the full range of ages, sexes, races, and other factors that could influence health status or the development of disease. To resolve this issue, specific exposed populations could be identified and evaluated if such research appears to be feasible.

5.10.5.4. Summary--

There are some serious methodological problems in the human studies literature that meke results equivocal. These problems are not necessarily insurmountable. But, at present, the data on human beings exposed to RF radiation is not yet sufficiently developed to be very useful in determining exposure limits for the general population.

TABLE 5-31. SUMMARY OF SELECTED HUMAN STUDIES CONCERNING EFFECTS OF RF-RADIATION EXPOSURE

Effects	Species	Exposure Conditions				Reference
		Frequency (MHz)	Intensity (mW/cm²)	Duration (Years)	SAR (W/kg) (est)	
No significant change in health status of exposed personnel	Human adult male	400 (PW) 2,880 (PW) 9,375 (PW)	~4 ~4 (avg) ~4 (avg)	0-13	~0.16 ~0.12 ~0.12	Barron and Baraff 1958 (See also Barron et al. 1955)
No differences in three major diagnostic categories between the two groups of microwave workers	Human adult male	Radar	<0.2 (avg) >0.2 (avg) 6.0 (max)	1-10	$<8\times10^{-3}$ $>8\times10^{-3}$ .24 (max)	Czerski et at. 1974; Siekierzynski et al. 1974a, 1974b
No differences observed in clinical evaluations. More subjective complaints in exposed group	Human adult male	Radar	<5	5-10	<0.2	Djordjevic et al. 1979
No effect on life span or cause of death	Human adult male and female	2,560-4,100 600-9,500	0.005 (max) 0.018 (max)	22* 0.5	2×10^{-4} (max) 7×10^{-4} (max)	Lilienfeld et al. 1978
No effect on mortality in a military population followed for more than 20 years	Human adult male	200-5000 (est, PW)	~1 (routine) 100 (occasional)	2	≤ 0.05 ≤ 5	Robinette et al. 1980
Decreased number of sperm/ml of ejaculate Reduced percentages of normal and motile sperm in ejaculate	Human adult male	3,600-10,000	Tens to hundreds μW/cm²	1-17 8 (avg)	$0.3\text{-}4\times10^{-2}$	Lancranjan et al. 1975

---

*Number of years of irradiation of the embassy and length of the study period, but the average exposure of individuals is estimated to be 2-4 years.

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Biological Effects of Radiofrequency Radiation

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NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the risk of existing and new man-made environmental hazards is necessary to establish sound regulatory policy. Environmental regulations enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our nation's population.

The Health Effects Research Laboratory conducts a coordinated environmental health research program in toxicology and clinical studies. These studies address problems in air pollution, radiofrequency radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory participates in the development and revision of air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is primarily responsible for providing the health basis for radiofrequency radiation guidelines. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator.

The intent of this document is to provide a comprehensive review of the scientific literature on the biological effects of radiofrequency radiation. The purpose of this effort is to evaluate critically the current state of knowledge for its pertinence and applicability in developing radiofrequency-radiation exposure guidelines for the general public.

F. G. Hueter, Ph.D.
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ABSTRACT

This document presents a critical and comprehensive review of the available literature on the biological effects of radiofrequency (RF) radiation through 1980. The objective is to determine whether the existing data base can contribute to the formulation of RF-radiation exposure guidance for the general public.

The frequency range of concern in this document is 0.5 MHz to 100 GHz, which includes all the significant sources of population exposure to RF radiation. Research reports that are judged to be credible according to a set of objective criteria are examined for the relation between the RF energy absorbed and the presence or absence of biological effects. The reported consequences of the interaction between RF radiation and biological systems are examined from four perspectives by 1) RF-energy-induced core temperature increases, 2) whole-body-averaged specific absorption rate (SAR), 3) the exogeneous energy burden as a percentage of resting metabolic rate, and 4) actual human experiences documented in epidemiological studies.

The existing data base does lead to tentative conclusions about the relation between RF-radiation exposure and biological effects that may serve as unadjusted upper limits for population exposure guidance; however, the uncertainties and unknowns in the current state of knowledge are potentially significant.

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SECTION 6

ASSESSMENT

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There are several approaches available for examining the interaction between RF energy and biological systems. The biological consequences may be assessed in terms of (1) their association with RF-energy-induced elevations of core temperature, (2) whole-body-averaged energy absorption rate (SAR), (3) the exogenous RF-energy burdens as a percentage increase over the resting metabolic rate (RMR), and (4) human effects provided by epidemiological and clinical studies.

None of these approaches is entirely satisfactory. The "temperature increase vs. biological effect relationship" fails to explain effects that have been observed in the absence of detectable increases in temperature. It is also limited because of incomplete knowledge of the body's response to localized increases in temperature, and because core temperature is not the most sensitive indicator of the quantity of absorbed external energy (Adair and Adams 1980b). The SAR is currently a limited concept because, as typically used, it is an estimation of absorbed energy as averaged over the whole-body mass. It does not address the implications of the existence of localized areas of increased energy deposition in exposed biological systems, or the considerable differences between species in their capacity to regulate a given energy burden. The RMR, although reflecting species differences in the internal production of energy, is limited in that it is also an average value for the whole body. Epidemiological and clinical studies suffer primarily from inadequate dosimetry, small numbers of subjects, and confounding environmental variables, which may affect the assessment end points. Nevertheless, we shall employ each of these approaches to the limits of their applicability in an attempt to determine whether the existing data base can contribute to the formulation of RF-radiation exposure guidance for the general public.

6.1 CORE TEMPERATURE

Heating is the least controversial explanation for RF-radiation effects at high exposure levels. It seems appropriate, therefore, to begin by examining RF-radiation exposures associated with quantifiable heat-related phenomena. The applicability of core-temperature increases as the controlling factor for population RF-radiation exposure has been considered by Tell and Harlen (1979).

The average rectal (core) temperature is approximately 37.0 °C (98.6 °F) for humans and most mammals. Prolonged elevation of a core temperature at 42 °C (107 °F) is associated with heat stroke and brain lesions; the temperature 41.2 °C (106.2 °F) occurs in only 1 of 1000 humans during fever (Folk 1974).

With RF-radiation exposures, even brief periods (15 to 20 min) at core temperatures of 41.5 to 42.5 °C in rats can result in increased fetal resorptions, decreased fetal body weights (Chernovetz et al. 1977), and significant red blood cell (RBC) hemolysis and K^+ efflux in adult rats (Peterson et al. 1979). In healthy young men whose mean body temperature was increased to 41 °C by RF-radiation exposure for up to 3 h, sperm numbers had decreased 60 percent by 40 to 60 days after treatment (MacLeod and Hotchkiss 1941). At this core temperature, temporary infertility in male rats has also been reported (Berman et al. 1980).

Berman et al. (1981) report that when RF-radiation exposure produces a maternal colonic temperature of < 41 °C in the pregnant rat, no effects are detectable in the fetus. O'Connor (1980) reached similar conclusions.

The mouse fetus is apparently more sensitive to increased maternal body temperature than is the fetal rat. Berman et al. (1978) report that a 0.8 °C temperature differential between exposed and sham-irradiated dams produced a 10 percent decrease in the body weight of the mouse fetus.

Several RF-radiation-induced effects have been reported for other stages of life in various animal species at core temperature increases of 1 to 3 °C. These include a stress-like response of the adrenal glands in irradiated infant rats (Guillet and Michaelson 1977); increased serum glucose and blood urea nitrogen (BUN) levels in adult rabbits (Wangemann and Cleary 1976); increased serum thyroxine and T_3 levels in dogs (Magin et al. 1977a,b); increases in circulating neutrophils and T and B lymphocytes in spleens of mice, along with a decrease in circulating lymphocytes (Liburdy 1977, 1979);

change in lymphocyte traffic between bone marrow, spleen, liver, and lung similar to that produced by stress-related steroids (Liburdy 1980); increased responsiveness of lymphocytes to mitogen stimulation in monkeys (Prince et al. 1972); increased white blood cell (WBC) count and decreased ^{59}Fe uptake in mice (Rotkovska and Vacek 1975); decreased exploratory activity of rats (Hunt et al. 1975); decreased vigilance in monkeys (de Lorge 1976); and work stoppage in rats (D'Andrea et al. 1977).

Core temperature increases of 1 to 2 °C are reported to be associated with decreased serum thyroxine and corticosteroid levels (Lu et al. 1977). Michaelson et al. (1964) found hemoconcentration and decreased lymphocyte, neutrophil, and eosinophil levels over a $\Delta T = +1.0$ to 1.7 °C in dogs. Djordjevic and Kolak (1973) observed increases in RBC, hematocrit, and hemoglobin at a $\Delta T = +1.0$ °C in rats, which may also be a case of hemoconcentration. Pazderova-Vejlupkova and Josifko (1979) more recently report decreases in the hematocrits, WBC, and lymphocyte numbers at $\Delta T = +0.5$ °C.

Below a 0.5 °C rise in core temperature, current research predominantly, although not unanimously, reports no detectable effects on reproduction, fetal weight, growth, development, hematological and immunological end points, hormone levels, and clinical blood chemistry (Berman et al. 1978, 1980; Johnson et al. 1978; Michaelson et al. 1978; Guillet and Michaelson 1977; Djordjevic et al. 1977; Smialowicz et al. 1979b; Milroy and Michaelson 1972; Lovely et al. 1977; Wangemann and Cleary 1976). Considering the collective evidence, but without accounting for population variables such as age, sex, and health, it could be argued that RF-radiation exposure levels should produce a transient core temperature increase of no more than 0.5 °C. This increase is within normal oscillations of human temperature between the sleeping state and the height of daily physical activity (Cahn et al. 1968). Furthermore, a transient core temperature of 37.5 °C is below the heat Threshold Limit Value of 38 °C for deep body temperature to which, it is believed, nearly all workers may be repeatedly exposed without adverse health effects (American Conference of Governmental Industrial Hygienists 1980).

Spiegel et al. (1980a) have developed numerical procedures that describe the human body's thermal response under various conditions of electromagnetic-radiation exposure. This thermal model, although based on sound physiological and physical foundations, has not yet been experimentally verified. However, it predicts that, under the worst-case exposure conditions, for a free-space resonant frequency of 80 MHz or a ground plane resonant frequency of 40 MHz for the 50th-percentile man (Diffrient et al. 1974), the power density required to produce a core temperature rise of 0.5 °C would be approximately 6 mW/cm^2 (Figure 6-1). The model also predicts a 3.6 °C rise in the internal temperature of the lower thigh at this power density exposure. The model cannot presently provide similar estimates for 1-, 5-, 10-, and 70-year-old humans.

6.2 SPECIFIC ABSORPTION RATE

There are considerable data on the biological effects of RF-radiation exposure that do not include core temperature measurements as one of the experimental parameters. However, these studies nearly always specify the

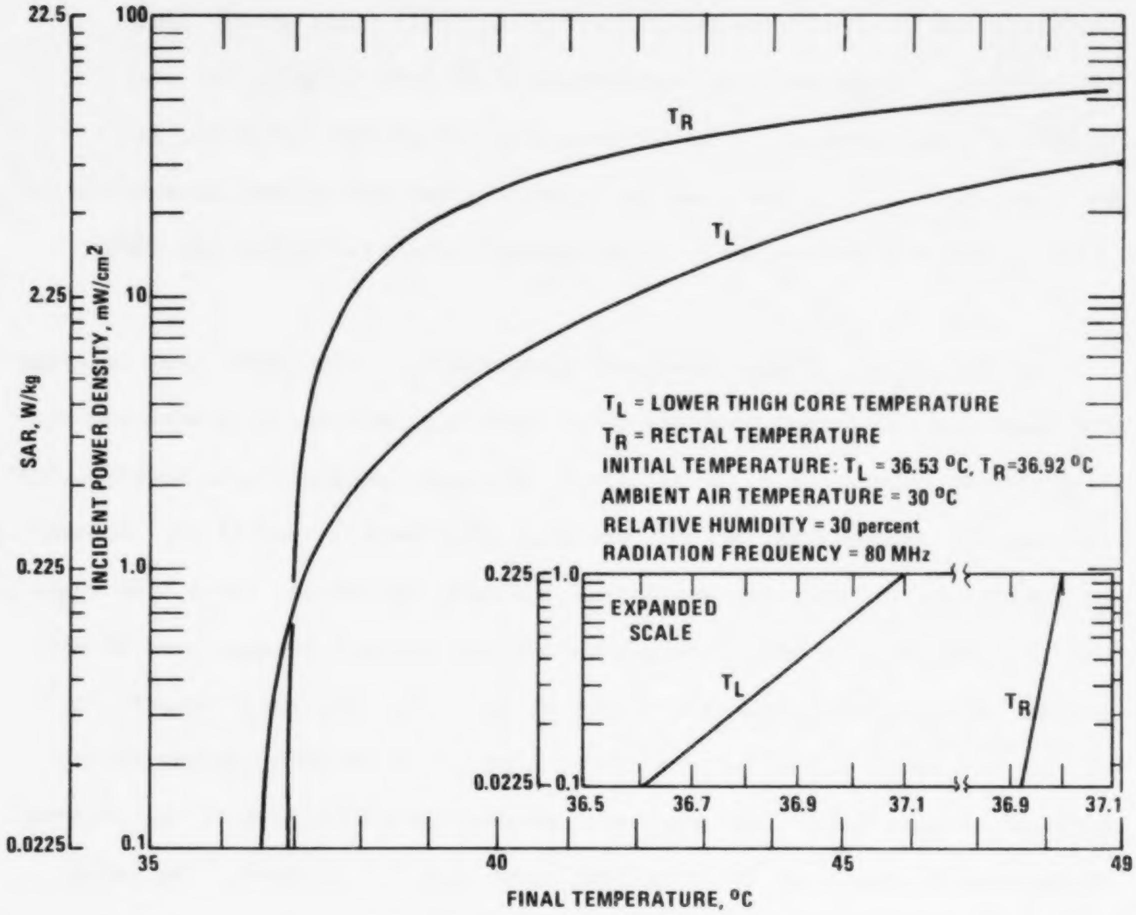

Figure 6-1. Steady-state temperature vs. SAR and power density.

frequency and power density of the field. Individually, neither parameter provides a reasonable correlate with biological effects, because RF-energy absorption is known to depend on the relation between wavelength and absorber size and orientation. However, when frequency and power density are combined with a knowledge of absorber size and dielectric property, an estimate of SAR can be made. The SAR is currently the parameter used most frequently to describe the RF-radiation energy absorbed by a biological system. It may also be employed as a correlate for the observed biological responses.

If one considers only the basic relation between the measured or estimated SAR's and the reported effects, the data cited in the preceding chapters show that SAR values near 100 W/kg are associated with effects on mammalian systems such as increased embryonic and fetal resorptions, birth defects, postnatal weight decrements, and reduced survival upon re-irradiation of the offspring of mice exposed during pregnancy (Rugh 1976a; Rugh *et al*. 1975). With other biological systems, such as *Drosophila* (Hamnerius *et al*. 1979), bacterial cells (Blackman *et al*. 1975), or biopolymers (Hamrick 1973; Allis 1975), no effects are usually reported.

Most of the information in the literature we have considered is derived from studies whose authors have reported or estimated SAR's at or below 45 W/kg. Experimental protocols using SAR's in the range 10 to 45 W/kg primarily involve brief (several minutes) exposures. Even at these high rates of energy absorption, the *in vitro* studies have shown few effects on the irradiated systems if temperature is properly controlled, e.g., no mutation induction in bacteria (Blackman *et al*. 1976; Dutta *et al*. 1979a, 1980; Corelli *et al*. 1977); no effects on enzyme activities (Ward *et al*. 1975; Bini *et al*. 1978; Allis and Fromme 1979); no effects on the physical characteristics and structure of biomolecules such as nucleic acids and proteins (Corelli *et al*. 1977; Allis 1975; Allis *et al*. 1976); and no change in lymphocyte transformation (Smialowicz 1976). Notable exceptions are Ismailov's (1971, 1977, 1978) reports that the human RBC exhibits increased electrophoretic mobility, K^+ efflux, Na^+ influx, and hydrogen exchange at SAR's between 10 and 45 W/kg; and Seaman and Wachtel's (1978) observation of a threshold at 7 W/kg for the increased firing rate of Aplysia pacemaker neurons.

Intact mammalian systems have generally been found to be affected by SAR's in the 10- to 45-W/kg range, even when the exposures have been short (minutes to hours). Lethal effects for pregnant rats have been reported by Chernovetz *et al*. (1977), along with fetotoxic effects (Berman *et al*. 1978). Some components of the immune system appear to react with an increased response, whereas others demonstrate diminished responses. Those components reported to increase are PMN levels (Kitsovskaya 1964; Michaelson *et al*. 1964; Lappenbusch *et al*. 1973; Liburdy 1977); splenic lymphocytes (Wiktor-Jedrzejczak *et al*. 1977a,b,c; Sulek *et al*. 1980); lymphocyte response to mitogen stimulation (Huang and Mold 1980; Wiktor-Jedrzejczak *et al*. 1977a,b,c); and lymphocyte transformation to the lymphoblast stage (Huang *et al*. 1977).

Roszkowski *et al*. (1980) recently reported a general immunosuppressive effect at 35 W/kg. These workers found an increase in lung cancer colonies and an inhibition of contact sensitivity to oxazolone in mice. Decreases are also reported in the primary antibody response to sheep red blood cell (SRBC) (Wiktor-Jedrzejczak *et al*. 1977a,b,c), the CFU for the erythroid granulocyte-macrophage series in bone marrow (Huang and Mold 1980), lymphocyte traffic from lung to spleen (Liburdy 1980), and circulating lymphocyte levels (Lappenbusch *et al*. 1973; Liburdy 1977).

Some biological end points appear to be unaffected even at 10 to 45 W/kg; e.g., postnatal survival, adult body weight, and longevity (Guillet and Michaelson 1977; Spalding et al. 1971) as well as the incidence of chromosome aberrations (McRee et al. 1978; Huang et al. 1977). Varma and Traboulay (1976) do, however, report changes in the physical properties of DNA extracted from the testes of mice exposed to 15 to 65 W/kg for 80 min.

Approximately 75 percent of the experimental studies that met the criteria for inclusion in this document employed SAR's $\leq$ 10 W/kg. Since the current data base deals with a limited range of biological variables and exposure durations when these studies are differentiated by observed "effects" (without regard to biological significance) or "no effects," and arranged within these two groupings by decreasing SAR values (Tables 6-1 and 6-2), a dichotomy becomes quite evident. A break point appears to occur at about 6 W/kg. Nearly all of the "no effects" data are associated with SAR's $\leq$ 6 W/kg regardless of species, exposure duration, or mode of exposure. This implies that "effects" are more likely for SAR's $\geq$ 6 W/kg.

Below 6 W/kg there exists a "gray" area in which both positive and negative results are reported. Nearly 90 percent of "effects" cited as occurring at < 6 W/kg involve behavioral, hematological or immunological elements, central nervous system structure and/or function, or hormone levels.

The range 0.4 to 6.0 W/kg appears to represent a transition zone from a range in which "effects" are highly likely (> 6 W/kg) to one in which properly designed, duplicative experiments, conducted by competent investigators

TABLE 6-1. STUDIES REPORTING "NO EFFECTS" AT SAR'S ≤ 10 W/kg
GROUPED BY BIOLOGICAL VARIABLE

Biological Variable	Relevant Studies	SAR's
Growth (Food, Water Intake)	Stavinoha *et al*. (1975)	6.3
	McAfee *et al*. (1973)	6.0-8.0
	Kaplan (1981)	3.4
	Michaelson *et al*. (1978)	2.5-10.0
	Johnson *et al*. (1978)	2.5
	Lovely *et al*. (1977)	1.0-2.5
	D'Andrea *et al*. (1979)	1.0-2.5
Behavior	D'Andrea *et al*. (1976)	5.0-6.0
	Moe *et al*. (1976)	3.9
	Mitchell *et al*. (1977)	2.3
	Sanza and de Lorge (1977)	2.1-4.7
	Gage (1979a)	0.3
	Scholl and Allen (1979)	1.6
	de Lorge (1976)	1.1-1.4
	Lovely *et al*. (1977)	1.0
	Roberti *et al*. (1975)	0.2-8.3
	Schrot *et al*. (1980)	0.2
	Thomas *et al*. (1979)	0.2
Mortality/Life Span	Kaplan (1981)	3.4
	Johnson *et al*. (1978)	2.5
	Spalding *et al*. (1971)	1.7
Hematology/Immunology	Smialowicz *et al*. (1979b)	> 4.0
	Liburdy (1980)	3.8
	Smialowicz (1981a)	2.0-3.0
	Spalding *et al*. (1971)	1.7
	Djordjevic *et al*. (1977)	1.0
Mutations/Chromosomal Aberrations	Blackman *et al*. (1975, 1976)	0.08-7.5
	McLees *et al*. (1972)	1.3
	Berman *et al*. (1980)	0.9
Teratology	Johnson *et al*. (1978)	2.5
	Berman *et al*. (1978)	2.0-8.1
Litter Size	Michaelson *et al*. (1978)	2.5-10.0
	Johnson *et al*. (1978)	2.5
Organ Weight	Michaelson *et al*. (1978)	2.5-10.0
	Mikolajczyk (1976)	1.0-2.0

(continued)

TABLE 6-1. (continued)

Biological Variable	Relevant Studies	SAR's
Blood Chemistry	Wangemann and Cleary (1976)	0.8
Fertility	Berman et al. (1980)	1.0-2.0
Hormones	Mikolajczyk (1976)	1.0-2.0
	Parker (1973)	2.0-6.5
	Lu et al. (1977)	2.5
	Milroy and Michaelson (1972)	0.25-2.5
Neurotransmitter Levels	Merritt et al. (1976)	3.0
Metabolic Rate	Ho and Edwards (1977a,b)	5.5

TABLE 6-2. STUDIES WITH REPORTED "EFFECTS" AT SAR'S $\leq$ 10 W/kg
GROUPED BY BIOLOGICAL VARIABLE

Biological Variable	Relevant Studies	SAR's
Behavior	de Lorge (1976)	5.0
	Moe et al. (1976)	3.6
	Gage et al. (1979)	2.7
	de Lorge and Ezell (1980)	2.5-4.9
	D'Andrea et al. (1980)	2.5
	Mitchell et al. (1977)	2.3
	Thomas et al. (1975)	1.4-1.5
	D'Andrea et al. (1979)	1.2
	Stern et al. (1979)	1.1
	Thomas et al. (1976)	1.1
	Rudnev et al. (1978)	1.0
	Adair and Adams (1980a,b)	1.0
	Schrot et al. (1980)	0.7
	Frey and Feld (1975)	0.4
Central Nervous System	Seaman and Wachtel (1978)	7.0
	Albert and DeSantis (1975,1976)	5.0-12.5
	Switzer and Mitchell (1977)	2.3
	Albert et al. (1979b)	2.0
	Goldstein and Sisko (1974)	0.1-0.3
	Baranski (1972b)	0.4-2.5

(continued)

TABLE 6-2. (continued)

Biological Variable	Relevant Studies	SAR's
Hematology/Immunology	Sulek *et al*. (1980)	5.0-11.8
	Smialowicz (1979a, 1982)	5.0-7.0
	Liburdy (1979)	4.6
	Michaelson *et al*. (1964)	4.0-6.0
	Huang and Mold (1980)	3.6-10.0
	Huang *et al*. (1977)	2.3-30.7
	Djordjevic and Kolak (1973)	2.0
	Deichmann *et al*. (1963)	1.5-2.2
	McRee *et al*. (1980a)	1.5
	Czerski (1975)	0.5-0.8
	Szmigielski *et al*. (1975)	0.5
	Baranski (1971)	0.5
	Prince *et al*. (1972)	0.4-2.0
Hormones	Lu *et al*. (1977)	5.0
	Lotz and Michaelson (1978)	3.0-12.8
	Mikolajczyk (1976)	1.0-2.0
Drug Potentiation	Edelwejn (1968)	1.0
	Thomas and Maitland (1979)	0.2
Mutations/Chromosome Aberrations	Manikowska *et al*. (1979)	0.05-5.0
Neurotransmitter Levels	Merritt *et al*. (1977)	6.0
Fertility	Berman *et al*. (1980)	5.6
Clinical Chemistry	Wangemann and Cleary (1976)	1.6-4.0

examining the same or similar end points, produce inconsistent results. The increased variability of results may suggest that this zone is at the lower limit of the effective SAR for some biological end points.

In § 3.2 (RF Field Interactions with Biological Systems), one of the major determinants of SAR is the relation between the wavelength of the electromagnetic radiation and the length of the object being irradiated.

Resonance, the optimal coupling of energy into an absorber, occurs when the object is nearly one-half the wavelength of the incident energy. The resonant frequencies for the general population range from approximately 40 to 190 MHz for two main reasons: body length varies with age, and the length of an object (acting as an antenna) is effectively doubled when the object is in contact with a conducting ground plane. When in free space or insulated from ground, the antenna length is equal to the physical length. Exposure at resonant frequencies represents a worst case, since the greatest absorption occurs at these frequencies (wavelengths) for a given exposure level. The average SAR for the resonant frequency in a ground-plane exposure is about 25 percent greater than for the free-space resonant frequency (Durney _et_ _al_. 1978). But, in view of other more significant simplifications used in this document, we have chosen to consider the SAR's and the associated exposures (mW/cm^2) to be equivalent for both exposure conditions.

Based on this viewpoint, a conservative limit for SAR would be 0.4 W/kg. An SAR of 0.4 W/kg may be converted to corresponding power densities for human infants, children, and adults by using the RF-radiation dosimetry data developed by Durney _et_ _al_. (1978); examples are given in Table 6-3.

6.3 RESTING METABOLIC RATE

The whole-body averaged SAR identifies the rate of exogenous energy input to a system in units of watts per kilogram. Although SAR does not necessarily equate with heating, the impact of a given SAR will, to an extent, be governed by the thermoregulatory capacity of the system.

TABLE 6-3. EQUIVALENT POWER DENSITY FOR FIVE AGES AND MASS SIZES AT RESONANT FREQUENCY FOR SAR = 0.4 W/kg*

			Resonant Frequency	
Age	Average Mass (kg)	Power Density (mW/cm^2)	Free Space (MHz)	Ground Plane (MHz)
1	10.0	1.2	190	95
5	19.5	1.1	140	70
10	32.2	1.2	95	50
Adult female	61.0	1.7	80	40
Adult male	70.0	1.7	80	40

*Data are from Durney _et al_. (1978).

The RMR is a measure of endogenous energy production. Although it varies widely for mammalian species, it has an established correlation with body mass (M), i.e., RMR = $3.86\ M^{-0.24}$ W/kg (Kleiber 1975). Examples of this relationship are listed below:

Species	Average Mass (kg)	RMR (W/kg)
Mouse	0.03	9.0
Rat	0.30	5.1
Squirrel monkey	1.10	3.8
Rhesus monkey	4.20	2.7
Man	70.00	1.4

RMR is also a function of several other variables, including age, sex, and activity. For human beings, Ruch and Patton (1973) report the following data:

Age (years)	Average Mass (kg)	RMR (W/kg)
1	10.0	2.8
5	19.5	2.5
10	32.2	2.0
20-24 (female)	61.1	1.2
20-24 (male)	70.0	1.3

Since species, body mass, and age are key factors in RMR, an RF-radiation exposure that results in a given SAR will have different numerical relationships to RMR for different species and ages. For example, an SAR of 2.0 W/kg has the following approximate relationships to a subject's RMR:

RMR (%)	Subject
150	Adult male human
100	10-year-old child
70	1-year-old child
50	Squirrel monkey
40	Rat
20	Mouse

A major consideration in the implications of absorbed RF energy is the mammalian system's ability to regulate the additional load; again, species plays an important role. The metabolic rate for a young adult male human varies by approximately a factor of 8 from 1.3 W/kg when resting to 11 W/kg for maximum sustained exercise (Kleiber 1975). The corresponding range of metabolic rates for a rat varies only by a factor of approximately 3 (Taylor et al. 1970). The span of metabolic rates accompanying various physical activities reflects the thermoregulatory latitude of different species in dealing with internally generated energy. But it is not known whether these thermoregulatory ranges also apply to the ability to handle RF energy absorbed from external sources.

To be consistent with the conservative approach we have taken in examining the other biological aspects of RF-energy absorption (i.e., core temperature and SAR), it is appropriate to discuss the lowest SAR's that have been reported to activate a thermoregulatory response in human beings and laboratory animals (e.g., increase evaporative heat loss [EHL], decrease metabolism, or elevate skin temperature). Using a mathematical modeling technique, Spiegel et al. (1979) found that an SAR of approximately 0.23 W/kg will increase EHL in the young adult human male exposed at 80 MHz, a whole-body resonance frequency. This SAR is equal to about 20% of the RMR of a young adult male. Models are not currently available to predict responses in humans of other ages. One could assume that an SAR of 0.23 W/kg will activate EHL in humans of all ages, or, since RMR varies with age, one could assume that an SAR equal to about 20% of the RMR will activate a thermoregulatory response. Support for the latter assumption is presented in Figure 6-2 (Gordon 1982a). Here an analysis of a variety of thermoregulatory responses in both human beings (models) and laboratory animals shows that a linear relation exists between the log of body mass and log of the SAR for the onset of a thermoregulatory response. It is important to note that Figure 6-2 was constructed from data from a number of laboratory studies that used different exposure techniques and environmental conditions. Variables such as physiologic parameter, ambient temperature, humidity, and age, to name a few, should affect the slope and intercept of the regression line (Gordon 1982a). For the human mass range (10 to 80 kg, the

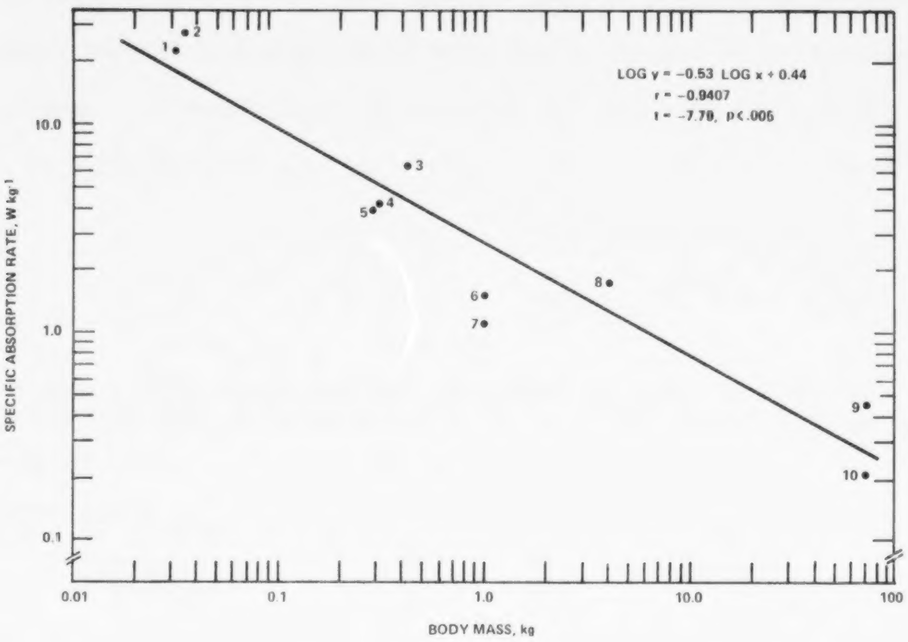

Figure 6-2. Relationship of body mass to the SAR necessary to alter the activity of various physiologic systems. Each datum represents the minimal SAR necessary to alter a physiologic response. Ambient temperature in these studies ranged from 20 to 35 °C. The number adjacent to each data point corresponds to the species, physiologic parameter, frequency, and literature reference, respectively:

(1) Mouse; inhibit metabolism; 2450 MHz; Ho and Edwards 1977b.
(2) Mouse; increase EHL; 2450 MHz; Gordon 1982a.
(3) Rat; inhibit metabolism; 2450 MHz; Phillips *et al*. 1975b.
(4) Rat; increase serum corticosterone; 2450 MHz; Lu *et al*. 1981.
(5) Rat; increase serum corticosterone; 2450 MHz; Lotz and Michaelson 1978.
(6) Squirrel monkey; increase skin blood flow; 2450 MHz; Adair and Adams 1980a.
(7) Modify thermoregulatory behavior; 2450 MHz; Adair and Adams 1980b.
(8) Rabbit; raise heart rate; 2450 MHz; Birenbaum *et al*. 1975.
(9) Man (model); increase EHL; 200 MHz; Spiegel *et al*. 1980a.
(10) Man (model); increase EHL; 80 MHz; Spiegel *et al*. 1979.

graph predicts that SAR's about 25% of the RMR are required to activate a thermoregulatory response. The associated power density exposures at resonant frequencies are from 1.2 to 2.6 mW/cm^2 (Table 6-4). Note that we chose to list in Table 6-4 the extrapolated SAR value from Figure 6.2 for the young adult male rather than the lower SAR predicted by the mathematical model. The equivalent power density at resonance is not significantly lower (1.3 vs. 0.9 mW/cm^2).

TABLE 6-4. THE INCREASED RMR AND EQUIVALENT SAR AND POWER DENSITY PREDICTED TO BE ASSOCIATED WITH THE ONSET OF HUMAN THERMOREGULATORY RESPONSE

Age (years)	Average body mass (kg)	RMR (%)	Equivalent SAR (W/kg)	Equivalent power density at resonant frequency* (mW/cm^2)
1	10.0	29	0.81	2.6
5	19.5	23	0.57	1.6
10	32.2	22	0.44	1.3
20-24 (female)	61.0	26	0.31	1.3
20-24 (male)	70.0	22	0.29	1.3
70 (female)	70.0	22	0.29	1.3
70 (male)	80.0	26	0.27	1.2

*Durney _et al_. 1978.

6.4 HUMAN STUDIES

Human data is a source of information that must be considered in the development of exposure guidelines. As stated earlier, most of the recorded observations of the effects of RF-radiation exposure on human beings have been provided by Soviet and other East European scientists. Because these are primarily clinical studies, rather than examinations of specific diseases with subsequent correlation with RF-radiation exposures, their utility is limited. Many of the same shortcomings are seen in the U.S. and Western European literature.

Most of the studies that provide sufficient technical detail have dealt with human populations exposed to low levels of RF radiation without detecting any effects. Lilienfeld _et_ _al_. (1978) found no effect on life span or cause of death in persons exposed to RF radiation over a period of years. Robinette _et_ _al_. (1980) also found no effect on life span, morbidity, or cause of death in adult males occupationally exposed to radar for periods up to 4 years. Cleary _et_ _al_. (1965) found no association between cataract formation and occupational exposure, and Cohen _et_ _al_. (1977) report no correlation between paternal exposure to RF radiation for several years and Down's Syndrome (mongolism) in their offspring. A comprehensive medical surveillance program conducted by an aircraft manufacturer did not detect any significant changes in the health status of 335 employees exposed to average power densities > 4 mW/cm^2 of 0.4- to 8-GHz radar (SAR > 0.12 W/kg, Barron and Baraff 1958).

The health effects data base has been examined from four different perspectives to determine whether specific limits might be indicated. As noted previously, no one perspective is complete, but this exercise employing all the available approaches is instructive. Human studies, the fourth perspective, are few in number and have as a principal weakness inadequate information on RF-radiation exposure, but do not indicate any obvious relationship between low level exposure and increased mortality or morbidity. Thus no reasonable estimate of an upper exposure limit can be derived from human studies. Table 6-5 presents the estimates for an upper limit for exposure levels from three of the four perspectives unadjusted for considerations of sex, health status, uncertainty, etc. These estimates range from 1.1 to 6.0 mW/cm^2 at resonant frequencies.

TABLE 6-5. SUMMARY OF ESTIMATES OF UNADJUSTED LIMITS FOR RF-RADIATION EXPOSURE AT RESONANT FREQUENCIES

		Corresponding Power Density Exposures (mW/cm^2)				
Parameter	Limit	1 year old	5 years old	10 years old	20 to 24 years old	70 years old
Core temperature	< 0.5 °C 1.4 W/kg	*	*	*	6.0	*
SAR not likely to be associated with "effects"	0.4 W/kg	1.2	1.1	1.2	1.7	1.7
Onset of thermoregulatory response	25% of RMR 0.8-0.3 W/kg	2.6	1.6	1.3	1.3	1.2

* = Data not available.

REFERENCES

Abramson, D. I., A. J. Harris, and P. Beaconsfield. 1957. Changes in Peripheral Blood Flow Produced by Short-Wave Diathermy. Arch. Phys. Med. Rehab., 38:369-376.

Adair, E. R., and B. W. Adams. 1980a. Microwaves Induced Peripheral Vasodilation in Squirrel Monkey. Science, 207:1381-1383.

Adair, E. R., and B. W. Adams. 1980b. Microwaves Modify Thermoregulatory Behavior in Squirrel Monkey. Bioelectromagnetics, 1:1-20.

Alam, M. T., N. Barthakur, N. G. Lambert, and S. S. Kasatiya. 1978. Cytological Effects of Microwave Radiation in Chinese Hamster Cells In Vitro. Can. J. Genet. Cytol., 20:23-30.

Albert, E. N. 1977. Light and Electron Microscopic Observations on the Blood-Brain Barrier after Microwave Irradiation. In: Symposium on Biological Effects and Measurement of Radio Frequency/Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026, Rockville, Maryland. pp. 294-304.

Albert, E. N. 1979a. Current Status of Microwave Effects on the Blood-Brain Barrier. J. Microwave Power, 14:281-285.

Albert, E. N. 1979b. Reversibility of Microwave-Induced Blood-Brain Barrier Permeability. Radio Sci., 14:323-327.

Albert, E. N., and M. DeSantis. 1975. Do Microwaves Alter Nervous System Structure? Ann. N.Y. Acad. Sci., 247:87-108.

Albert, E. N., and M. DeSantis. 1976. Histological Observations on Central Nervous System: In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 299-310.

Albert, E. N., and J. M. Kerns. 1981. Reversible Microwave Effects on the Blood-Brain Barrier. Brain Res., 230:153-164.

Albert, E., C. Blackman, and F. Slaby. 1980. Calcium Dependent Secretory Protein Release and Calcium Efflux During RF Irradiation of Rat Pancreatic Tissue Slices. In: Ondes Electromagnetiques et Biologie, A. J. Berteaud and B. Servantie, eds. Paris, France. pp. 325-329.

Albert, E. N., M. F. Sherif, N. J. Papadopoulos, F. J. Slaby, and J. Monahan. 1981. Effect of Nonionizing Radiation on the Purkinje Cells of the Rat Cerebellum. Bioelectromagnetics, 2:247-257.

Alfsen, A. , and A. J. Berteaud, eds. 1976. Water and Biological Systems, International Colloquia of the National Center for Scientific Research, No. 246, Paris, France. 321 pp.

Allen, S. J., W. D. Hurt, J. H. Krupp, J. A. Ratliff, C. H. Durney, and C. C. Johnson. 1976. Measurement of Radiofrequency Power Absorption in Monkeys, Monkey Phantoms, and Human Phantoms Exposed to 10-50 MHz Fields. In: Biological Effects of Electromagnetic Waves, Vol. II, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8011. pp. 83-95.

Allis, J. W. 1975. Irradiation of Bovine Serum Albumin with a Crossed-Beam Exposure-Detection System. Ann. N.Y. Acad. Sci., 247:312-322.

Allis, J. W., and M. L. Fromme. 1979. Activity of Membrane-Bound Enzymes Exposed to Sinusoidally Modulated 2450-MHz Microwave Radiation. Radio Sci., 14(6S):85-91.

Allis, J. W., M. L. Fromme, and D. E. Janes. 1976. Pseudosubstrate Binding to Ribonuclease During Exposure to Microwave Radiation at 1.70 and 2.45 GHz. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 366-376.

Allis, J. W., C. F. Blackman, M. L. Fromme, and S. G. Benane. 1977. Measurement of Microwave Radiation Absorbed by Biological Systems, 1, Analysis of Heating and Cooling Data. Radio Sci., 12(6S):1-8

American Conference of Governmental Industrial Hygienists. 1980. TLV's--Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1980. ACGIH, Cincinnati, Ohio.

Ames, B. N., J. McCann, and E. Yamasaki. 1975. Methods for Detecting Carcinogens and Mutagens with the Salmonella/Mammalian-Microsome Mutagenicity Test. Mutat. Res., 31:347-364.

Anderson, G. E., and J. B. Kinn. 1980. Microcomputer Calorimeter Controller (Abstract). Bioelectromagnetics, 1:239.

ANSI. 1974. An American National Standard, Safety Level of Electromagnetic Radiation with Respect to Personnel (C95.1-1974). American National Standards Institute, New York, New York.

ANSI. 1982. American National Standard Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 300 kHz-100 GHz (ANSI C95.1-1982). American National Standards Institute, New York, New York.

Appleton, B. 1973. Results of Clinical Surveys for Microwave Ocular Effects. HEW Publication (FDA) 73-8031. U.S. Dept. of Health, Education, and Welfare, Rockville, Maryland. 13 pp.

Appleton, B., and G. C. McCrossan. 1972. Microwave Lens Effects in Humans. Arch. Ophthal., 88:259-262.

Appleton, B., S. E. Hirsch, and P. V. K. Brown. 1975. Investigation of Single Exposure Microwave Ocular Effects at 3000 MHz. Ann. N.Y. Acad. Sci., 247:125-134.

Arber, S. L. 1976. Effect of Microwaves on Resting Potential of Giant Neurons of Mullusk Helix Pomatia. Electronnaya Obrabotka Materialov, 6:78-79.

Arehart-Treichel, J. 1974. Sperm Don't Like It Hot. Sci. News, 105:309-310.

Ashman, R. B., and A. J. Nahmias. 1978. Effect of Incubation Temperature on Mitogen Responses of Lymphocytes from Adult Peripheral Blood and from Cord Blood. Clin. Exp. Immunol., 33:319-326.

Aslan, E. E. 1970. Electromagnetic Radiation Survey Meter. IEEE Trans. Instrum. Meas., IM-19:368-372.

Aslan, E. 1976. A Low Frequency H-Field Radiation Monitor. In: Biological Effects of Electromagnetic Waves, Vol. 2, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8011. pp. 229-238.

Aslan, E. 1979. The Maturing of Electromagnetic Radiation Hazard Instruments. Microwave J., 22:83-90.

Atkinson, R. M. 1975. Screening Medicines for Teratogenicity: Problems of Interpretation. In: Teratology: Trends and Applications. C. L. Berry and D. E. Poswillo, eds. Springer-Verlag, New York, New York. pp. 136-146.

Austin, G. N., and S. M. Horvath. 1954. Production of Convulsions in Rats by High Frequency Electrical Currents. Am. J. Phys. Med., 33:141-149.

Baranski, S. 1971. Effect of Chronic Microwave Irradiation on the Blood Forming System of Guinea Pigs and Rabbits. Aerospace Med., 42:1196-1199.

Baranski, S. 1972a. Effect of Microwaves on the Reactions of the White Blood Cells System. Acta Physiol. Polon., 23:685-695.

Baranski, S. 1972b. Histological and Histochemical Effect of Microwave Irradiation on the Central Nervous System of Rabbits and Guinea Pigs. Am. J. Phys. Med., 51(4):182-191.

Baranski, S., and P. Czerski. 1976. Biological Effects of Microwaves. Dowden, Hutchinson, and Ross, Stroudsburg, Pennsylvania. 234 pp.

Baranski, S., and Z. Edelwejn. 1968. Studies on the Combined Effect of Microwaves and Some Drugs on Bioelectric Activity of Rabbit Central Nervous System. Acta Physiol. Polon., 19:31-41.

Baranski, S., K. Ostrowski, and W. Stodolnik-Baranska. 1972. Functional and Morphological Studies of the Thyroid Gland in Animals Exposed to Microwave Irradiation. Acta Physiol. Pol., 23:1029-1039.

Barber, D. E. 1962. The Reaction of Luminous Bacteria to Microwave Radiation Exposures in the Frequency Range of 2608.7-3082.3 Mc. IEEE Trans. Biomed. Electronics, BME-9:77-80.

Barber, P. W., O. P. Gandhi, M. J. Hagmann, and I. Chatterjee. 1979. Electromagnetic Absorption in a Multi-Layered Model of Man. IEEE Trans. Biomed. Eng., BME-26(7):400-405.

Barnes, F. S., and C. J. Hu. 1977. Model for Some Nonthermal Effects of Radio and Microwave Fields on Biological Membranes. IEEE Trans. Microwave Theory Techniques, MTT-25:742-746.

Barron, C. I., and A. A. Baraff. 1958. Medical Considerations of Exposure to Microwaves (Radar). J. Am. Med. Ass., 168:1194-1199.

Barron, C. I., A. A. Love, and A. A. Baraff. 1955. Physical Evaluations of Personnel Exposed to Microwave Emanations. J. Aviat. Med., 26: 442-452.

Bassen, H. 1977. Internal Dosimetry and External Microwave Field Measurement Using Miniature Electric Field Probes. In: Symposium on Biological Effects and Measurement of Radio Frequency/Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026, Rockville, Maryland. pp. 136-151.

Bassen, H., M. Swicord, and J. Abita. 1975. A Miniature Broad-Band Electric Field Probe. Ann. N.Y. Acad. Sci., 247:481-493.

Bassen, H., P. Herchenroeder, A. Cheung, and S. Neuder. 1977a. Evaluation of an Implantable Electric-Field Probe Within Finite Simulated Tissues. Radio Sci., 12(6S):15-25.

Bassen, H., W. Herman, and R. Hoss. 1977b. EM-Probe with Fiber Optic Telemetry System. Microwave J., 20:35-47.

Bassett, H. L., H. A. Ecker, R. C. Johnson, and A. P. Sheppard. 1971. New Techniques for Implementing Microwave Biological Exposure Systems. IEEE Trans. Microwave Theory Techniques, MTT-19(2):197-204.

Bawin, S. M., and W. R. Adey. 1976. Sensitivity of Calcium Binding in Cerebral Tissue to Weak Environmental Electric Fields Oscillating at Low Frequency. Proc. Natl. Acad. Sci. USA, 73:1999-2003.

Bawin, S. M., and W. R. Adey. 1977. Calcium Binding in Cerebral Tissues. In: Symposium on Biological Effects and Measurement of Radio Frequency/

Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026, Rockville, Maryland. pp. 305-313.

Bawin, S. M., R. J. Galavas-Medici, and W. R. Adey. 1973. Effects of Modulated Very High Frequency Fields on Specific Brain Rhythms in Cats. Brain Res., 58:365-384.

Bawin, S. M., L. K. Kaczmarek, and W. R. Adey. 1975. Effects of Modulated VHF Fields on the Central Nervous System. Ann. N.Y. Acad. Sci., 247:74-81.

Bawin, S. M., A. R. Sheppard, and W. R. Adey. 1978. Possible Mechanisms of Weak Electromagnetic Field Coupling in Brain Tissue. Bioelectrochemistry and Bioenergetics, 5:67-76.

Belkhode, M. L., D. L. Johnson, and A. M. Muc. 1974a. Thermal and Athermal Effects of Microwave Radiation on the Activity of Glucose-6-Phosphate Dehydrogenase in Human Blood. Health Phys., 26:45-51.

Belkhode, M. L., A. M. Muc, and D. L. Johnson. 1974b. Thermal and Athermal Effects of 2.8 GHz Microwaves on Three Human Serum Enzymes. J. Microwave Power, 9:23-29.

Belsher, D. R. 1975. Development of Near-Field Electric Energy Density Meter Model EDM-2. HEW Publication (NIOSH) 75-140, U.S. Department of Health, Education, and Welfare, Public Health Service, Cincinnati, Ohio. 61 pp.

Ben-Hur, E., M. M. Elkind, and B. V. Bronk. 1974. Thermally Enhanced Radioresponse of Cultured Chinese Hamster Cells: Inhibition of Repair of Sublethal Damage and Enhancement of Lethal Damage. Radiat. Res., 58:38-51.

Benzinger, T. H. 1969. Heat Regulation: Homeostasis of Central Temperature in Man. Physiol. Rev. 49:671-759.

Berman, E., J. B. Kinn, and H. B. Carter. 1978. Observations of Mouse Fetuses after Irradiation with 2.45 GHz Microwaves. Health Phys., 35:791-801.

Berman, E., H. B. Carter, and D. House. 1980. Tests of Mutagenesis and Reproduction in Male Rats Exposed to 2450-MHz (CW) Microwaves. Bioelectromagnetics, 1:65-76.

Berman, E., H. B. Carter, and D. House. 1981. Observations of Rat Fetuses after Irradiation with 2450-MHz (CW) Microwaves. J. Microwave Power, 16(1):9-13.

Bermant, R. I., D. L. Reeves, D. M. Levinson, and D. R. Justesen. 1979. Classical Conditioning of Microwave-Induced Hyperthermia in Rats. Radio Sci., 14(6S):201-207.

Bingham, P. M., R. H. Baltz, L. S. Ripley, and J. W. Drake. 1976. Heat Mutagenesis in Bacteriophage T4: The Transversion Pathway. Proc. Natl. Acad. Sci. USA, 73(11):4159-4163.

Bini, M., A. Checcucci, A. Ignesti, L. Millanta, N. Rubino, C. Camici, G. Manao, and G. Ramponi. 1978. Analysis of the Effects of Microwave Energy on Enzymatic Activity of Lactate Dehydrogenase (LDH). J. Microwave Power, 13:95-99.

Birenbaum, L., G. M. Grosof, S. W. Rosenthal, and M. M. Zaret. 1969a. Effect of Microwaves on the Eye. IEEE Trans. Biomed. Eng., BME-16:7-14.

Birenbaum, L., I. T. Kaplan, W. Metlay, S. W. Rosenthal, H. Schmidt, and M. M. Zaret. 1969b. Effect of Microwaves on the Rabbit Eye. J. Microwave Power, 4:232-243.

Birenbaum, L., I. T. Kaplan, W. Metlay, S. W. Rosenthal, and M. M. Zaret. 1975. Microwave and Infra-Red Effects on Heart Rate, Respiration Rate and Subcutaneous Temperature of the Rabbit. J. Microwave Power, 10:3-18.

Blackman, C. F., and J. A. Black. 1977. Measurement of Microwave Radiation Absorbed by Biological Systems, 2. Analysis by Dewar-Flask Calorimetry. Radio Sci., 12(6S):9-14.

Blackman, C. F., S. G. Benane, C. M. Weil, and J. S. Ali. 1975. Effects of Nonionizing Electromagnetic Radiation on Single-Cell Biologic Systems. Ann. N.Y. Acad. Sci., 247:352-366.

Blackman, C. F., M. C. Surles, and S. G. Benane. 1976. The Effect of Microwave Exposure on Bacteria: Mutation Induction. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 406-413.

Blackman, C. F., J. A. Elder, C. M. Weil, S. G. Benane, D. C. Eichinger, and D. E. House. 1979. Induction of Calcium-Ion Efflux from Brain Tissue by Radio-Frequency Radiation: Effects of Modulation Frequency and Field Strength. Radio Sci., 14(6S):93-98.

Blackman, C. F., S. G. Benane, J. A. Elder, D. E. House, J. A. Lampe, and J. M. Faulk. 1980a. Induction of Calcium-Ion Efflux from Brain Tissue by Radiofrequency Radiation: Effect of Sample Number and Modulation Frequency on the Power-Density Window. Bioelectromagnetics, 1:35-43.

Blackman, C. F., S. G. Benane, W. T. Joines, M. A. Hollis, and D. E. House. 1980b. Calcium-Ion Efflux from Brain Tissue: Power-Density Versus Internal Field-Intensity Dependencies at 50 MHz RF Radiation. Bioelectromagnetics, 1:277-283.

Blecha, F., R. A. Barry, and K. W. Kelley. 1982. Stress-Induced Alterations in Delayed-Type Hypersensitivity to SRBC and Contact Sensitivity to DNFB in Mice. Proc. Soc. Exp. Biol. Med., 169:239-246.

Blevins, R. D., R. C. Crenshaw, A. E. Hougland, and C. E. Clark. 1980. The Effects of Microwave Radiation and Heat on Specific Mutants of Salmonella typhimurium LT2. Radiat. Res., 82:511-517.

Blum, H. F. 1967. Effects of Ultraviolet Light on Man. In: Seminar on Human Biometeorology, J. Dicke, ed. Pub. Health Serv. Pub. 999-AP-25. pp. 109-120.

Boggs, R. F., A. P. Sheppard, and A. J. Clark. 1972. Effects of 2450 MHz Microwave Radiation on Human Blood Coagulation Processes. Health Phys., 22:217-224.

Bowler, K. 1972. The Effect of Repeated Applications of Heat on Spermatogenesis in the Rat: A Histological Study. J. Reprod. Fertility, 28: 325-333.

Bowman, R. R. 1970. Quantifying Hazardous Electromagnetic Fields: Practical Considerations. NBS Technical Note 389, U.S. Department of Commerce, National Bureau of Standards, Boulder, Colorado. 15 pp.

Bowman, R. R. 1976. A Probe for Measuring Temperature in Radio-Frequency-Heated Material. IEEE Trans. Microwave Theory Techniques, MTT-24:43-45.

Brodeur, P. 1977. The Zapping of America. W. W. Norton and Co., New York, New York. 343 pp.

Brown, J. L. 1975. The Evolution of Behavior. W. W. Norton and Co., New York, New York. 761 pp.

Buss, M. E., and S. A. Henderson. 1971. Induced Bivalent Interlocking and the Course of Meiotic Chromosome Synapsis. Nature New Biol., 234:243-246.

Cahn, H. A., G. E. Folk, Jr., and P. E. Huston. 1968. Age Comparison of Human Day-Night Physiological Differences. Aerospace Med., 39:608-610.

Cain, C. A., and W. J. Rissmann. 1978. Mammalian Auditory Responses to 3.0 GHz Microwave Pulses. IEEE Trans. Biomed. Eng., BME-25:288-293.

Cairnie, A. B., L. F. Prud'homme-Lalonde, R. K. Harding, and M. Zuker. 1980. The Measurement of Rectal and Testis Temperature in Conscious Mice, with Observations on the Effect of Direct Heating. Phys. Med. Biol., 25(2):317-322.

Carpenter, R. L. 1979. Ocular Effects of Microwave Radiation. Bull. N.Y. Acad. Med., 55:1048-1057.

Carpenter, R. L., and C. A. Van Ummersen. 1968. The Action of Microwave Radiation on the Eye. J. Microwave Power, 3:3-19.

Carpenter, R. L., D. K. Biddle, and C. A. Van Ummersen. 1960a. Biological Effects of Microwave Radiation, with Particular Reference to the Eye. In: Proc. Third Internat. Conf. on Medical Electronics, London. Medical Electronics, Part III:401-408.

Carpenter, R. L., D. K. Biddle, and C. A. Van Ummersen. 1960b. Opacities in the Lens of the Eye Experimentally Induced by Exposure to Microwave Radiation. IRE Trans. Med. Electronics, 7:152-157.

Carpenter, R. L., G. J. Hagan, and G. L. Donovan. 1977. Are Microwave Cataracts Thermally Caused? In: Symposium on Biological Effects and Measurement of Radio Frequency/Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026. pp. 352-379.

Carroll, D. R., D. M. Levinson, D. R. Justesen, and R. L. Clarke. 1980. Failure of Rats to Escape from a Potentially Lethal Microwave Field. Bioelectromagnetics, 1:101-115.

Carslaw, H. S., and J. C. Jaeger. 1959. Conduction of Heat in Solids, Clarendon Press, Oxford, England. pp. 230-231.

Catania, A. C., ed. 1968. Contemporary Research in Operant Behavior. Scott, Foresman, Glenview, Illinois. 358 pp.

Catravas, G. N. 1976. Styrofoam Cages for Rats used in Microwave Research: Coating with Quinine. Health Phys., 31:68-69.

Catravas, G. N., J. B. Katz, J. Takenaja, and J. R. Abbott. 1976. Biochemical Changes in the Brain of Rats Exposed to Microwaves of Low Power Density. J. Microwave Power, 11:147-148.

Chamness, A. F., H. R. Scholes, S. W. Sexauer, and J. W. Frazer. 1976. Metal Ion Content of Specific Areas of the Rat Brain after 1600 MHz Radio Rrequency Irradiation. J. Microwave Power, 11:333-338.

Chappuis, P., P. Pittet, and E. Jequier. 1976. Heat Storage Regulation in Exercise During Thermal Transients. J. Appl. Physiol., 40:384-392.

Chatterjee, I., M. J. Hagmann, and O. P. Gandhi. 1980. Electromagnetic Energy Deposition in an Inhomogeneous Block Model of Man for Near-Field Irradiation Conditions. IEEE Trans. Microwave Theory and Techniques, MTT-28:1452-1459.

Chen, K. C., and C. J. Lin. 1978. A System for Studying Effects of Microwaves on Cells in Culture. J. Microwave Power, 13:251-256.

Chen, K. M., and B. S. Guru. 1977. Induced EM Fields Inside Human Bodies Irradiated by EM Waves up to 500 MHz. J. Microwave Power, 12(2):173-183.

Chernovetz, M. E., D. R. Justesen, N. W. King, and J. E. Wagner. 1975. Teratology, Survival, and Reversal Learning after Fetal Irradiation of Mice by 2450-MHz Microwave Energy. J. Microwave Power, 10(4):391-409.

Chernovetz, M. E., D. R. Justesen, and A. F. Oke. 1977. A Teratological Study of the Rat: Microwave and Infrared Radiations Compared. Radio Sci., 12(6S):191-197.

Chernovetz, M. E., D. R. Justesen, and D. M. Levinson. 1979. Acceleration and Deceleration of Fetal Growth of Rats by 2450-MHz Microwave Radiation. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. Ottawa, Canada. pp. 175-193.

Chou, C. K., and R. Galambos. 1979. Middle-Ear Structures Contribute Little to Auditory Perception of Microwaves. J. Microwave Power, 14:321-326.

Chou, C. K., R. Galambos, A. W. Guy, and R. H. Lovely. 1975. Cochlear Microphonics Generated by Microwave Pulses. J. Microwave Power, 10:361-367.

Chou, C. K., A. W. Guy, and R. Galambos. 1976. Microwave-Induced Auditory Response: Cochlear Microphonics. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 89-103.

Chou, C. K., A. W. Guy, K. R. Foster, R. Galambos, and D. R. Justesen. 1980. Holographic Assessment of Microwave Hearing. Science, 209:1143-1144.

Christman, C. L., H. S. Ho, and S. Yarrow. 1974. A Microwave Dosimetry System for Measured Sampled Integral-Dose Rate. IEEE Trans. Microwave Theory Techniques, MTT-22(12):1267-1272.

Clapman, R. M., and C. A. Cain. 1975. Absence of Heart Rate Effects in Isolated Frog Heart Irradiated with Pulsed Modulated Microwave Energy. J. Microwave Power, 10:411-419.

Cleary, S. F. 1980. Microwave Cataractogenesis. Proc. IEEE, 68:49-55.

Cleary, S. F., and B. S. Pasternack. 1966. Lenticular Changes in Microwave Workers: A Statistical Study. Arch. Environ. Health, 12:23-29.

Cleary, S. F., B. S. Pasternack, and G. W. Beebe. 1965. Cataract Incidence in Radar Workers. Arch. Environ. Health, 11:179-182.

Cleary, S. F., and R. T. Wangemann. 1976. Effect of Microwave Radiation on Pentobarbital-Induced Sleeping Time. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 311-322.

Cogan, D. G., S. J. Fricker, M. Lubin, D. D. Donaldson, and H. Hardy. 1958. Cataracts and Ultra-High-Frequency Radiation. A.M.A. Arch. Ind. Health, 18:299-302.

Cohen, B. H., A. M. Lilienfeld, S. Kramer, and L. C. Hyman. 1977. Parental Factors in Down's Syndrome: Results of the Second Baltimore Case-Control Study. In: Population Cytogenetics--Studies in Humans, E. B. Hook and I. H. Porter, eds. Academic Press, New York, New York. pp. 301-352.

Conover, D. L., J. M. Lary, and P. L. Hanser. 1980. Thermal Threshold for Teratogenic Response in Rats Irradiated at 27.12 MHz (Abstract). Bioelectromagnetics, 1:204.

Constant, P. C., Jr. 1967. Hearing EM Waves. Digest of the Seventh International Conference on Medical and Biological Engineering, Bertil Jacobson, ed. Department of Medical Engineering, Karolinska Institute, Stockholm, Sweden. p. 349.

Cook, H. F. 1952. The Pain Threshold for Microwave and Infra-Red Radiations. J. Physiol., 118:1-11.

Corelli, J. C., R. J. Gutmann, S. Kohazi, and J. Levy. 1977. Effects of 2.6-4.0 GHz Microwave Radiation on E. coli B. J. Microwave Power, 12:141-144.

Crawford, M. L. 1974. Generation of Standard FM Fields Using TEM Transmission Cells. IEEE Trans. Electromagnetic Compatibility, EMC-16:189-95.

Crosbie, R. J., J. D. Hardy, and E. Fessender. 1963. Electrical Analog Simulation of Temperature Regulation in Man. In: Temperature, Its Measurement and Control in Science and Industry, Part III, J. H. Hardy, ed. Reinhold Publ., New York, New York. Ch. 55, p. 627.

Czerski, P. 1975. Microwave Effects on the Blood-Forming System with Particular Reference to the Lymphocyte. Ann. N.Y. Acad. Sci., 247:232-242.

Czerski, P., M. Sierkierzynski, and A. Gidynski. 1974. Health Surveillance of Personnel Occupationally Exposed to Microwaves. I. Theoretical Considerations and Practical Aspects. Aerospace Med., 45:1137-1142.

Daily, L., Jr., K. G. Wakim, J. F. Herrick, E. M. Parkhill, and W. L. Benedict. 1950a. The Effects of Microwave Diathermy on the Eye of the Rabbit. Am. J. Ophthalmol., 35:1001-1017.

Daily, L., Jr., K. G. Wakim, J. F. Herrick, E. M. Parkhill, and W. L. Benedict. 1950b. The Effects of Microwave Diathermy on the Eye. Am. J. Ophthalmol., 33:1241-1254.

D'Andrea, J. A., O. P. Gandhi, and R. P. Kesner. 1976. Behavioral Effects of Resonant Electromagnetic Power Absorption in Rats. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 257-273.

D'Andrea, J. A., O. P. Gandhi, and J. L. Lords. 1977. Behavioral and Thermal Effects of Microwave Radiation at Resonant and Nonresonant Wavelengths. Radio Sci., 12:251-256.

D'Andrea, J. A., O. P. Gandhi, J. L. Lords, C. H. Durney, C. C. Johnson, and L. Astle. 1979. Physiological and Behavioral Effects of Chronic Exposure to 2450-MHz Microwaves. J. Microwave Power, 14:351-362.

D'Andrea, J. A., O. P. Gandhi, J. L. Lords, C. H. Durney, L. Astle, L. J. Stensaas, and A. A. Schoenberg. 1980. Physiological and Behavioral Effects of Prolonged Exposure to 915 MHz Microwaves. J. Microwave Power, 15(2):123-135.

Dardalhon, M., D. Averbeck, and A. J. Berteaud. 1980. Action des Ondes Centimetriques Seules ou Combinees avec les Rayons Ultra Violets sur les Cellules Eucaryotiques. In: URSI International Symposium Proceedings, Ondes Electromagnetiques et Biologie, A. J. Berteaud and B. Servantie, eds. Paris, France. pp. 17-24.

Davidson, J. A., P. A. Kondra, and M. A. K. Hamid. 1976. Effects of Microwave Radiation on Eggs, Embryos and Chickens. Can. J. Anim. Sci., 56:709-713.

Deficis, A., J. C. Dumas, S. Laurens, and G. Plurien. 1979. Microwave Irradiation and Lipid Metabolism in Mice. Radio Sci., 14(6S):99-101.

Deichmann, W. B., E. Bernal, F. Stephens, and K. Landeen. 1963. Effects on Dogs of Chronic Exposure to Microwave Radiation. J. Occupational Med., 5:418-425.

Deichmann, W. B., J. Miale, and K. Landeen. 1964. Effect of Microwave Radiation on the Hemopoietic System of the Rat. Toxicol. Appl. Pharmacol., 6:71-77.

de Lorge, J. O. 1976. The Effects of Microwave Radiation on Behavior and Temperature in Rhesus Monkeys. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 158-174.

de Lorge, J. 1979. Disruption of Behavior in Mammals of Three Different Sizes Exposed to Microwaves: Extrapolation to Larger Mammals. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. Ottawa, Canada. pp. 215-228.

de Lorge, J. 1979. Operant Behavior and Rectal Temperature of Squirrel Monkeys During 2.45-GHz Microwave Irradiation. Radio Sci., 14(6S):217-225.

de Lorge, J. O., and C. S. Ezell. 1980. Observing-Responses of Rats Exposed to 1.28- and 5.62-GHz Microwaves. Bioelectromagnetics, 1:183-198.

Dietzel, F. 1975. Effects of Electromagnetic Radiation on Implantation and Intrauterine Development of the Rat. Ann. N.Y. Acad. Sci., 247:367-376.

Dietzel, F., and W. Kern. 1970. Abortion Following Ultra-Short-Wave Hyperthermia: Animal Experiments. Arch. Gynak., 209:237-255.

Dietzel, F., W. Kern, and R. Steckenmesser. 1972. Deformity and Intrauterine Death after Short-Wave Therapy in Early Pregnancy in Experimental Animals. Munch. Med. Wchschr., 114:228-230.

Diffrient, N., A. R. Tilley, and J. C. Bardagjy. 1974. Humanscale 1/2/3. The MIT Press, Boston, Massachusetts.

Djordjevic, Z., and A. Kolak. 1973. Changes in the Peripheral Blood of the Rat Exposed to Microwave Radiation (2400 MHz) in Conditions of Chronic Exposure. Aerospace Med., 44:1051-1054.

Djordjevic, Z., N. Lazarevic, and V. Djokovic. 1977. Studies on the Hematologic Effects of Long-Term, Low-Dose Microwave Exposure. Aviat. Space Environ. Med., 48:516-518.

Djordjevic, Z., A. Kolak, M. Stojkovic, N. Rankovic, and P. Ristic. 1979. A Study of the Health Status of Radar Workers. Aviat. Space Environ. Med., 50:396-398.

Drost-Hansen, W., and J. S. Clegg, eds. 1979. Cell-Associated Water, Academic Press, New York, New York. 440 pp.

Dumanskij, J. D., and M. G. Sandala. 1974. The Biologic Action and Hygienic Significance of Electromagnetic Fields of Superhigh and Ultrahigh Frequencies in Densely Populated Areas. In: Biologic Effects and Health Hazards of Microwave Radiation. P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess,and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 289-293.

Durney, C. H. 1980. Electromagnetic Dosimetry for Models of Humans and Animals: A Review of Theoretical and Numerical Techniques. Proc. IEEE, 68(1):33-40.

Durney, C. H., C. C. Johnson, P. W. Barber, H. Massoudi, M. F. Iskander, J. L. Lords, D. K. Ryser, S. J. Allen, and J. C. Mitchell. 1978. Radiofrequency Radiation Dosimetry Handbook, 2nd ed. Report SAM-TR-78-22, USAF School of Aerospace Medicine, Brooks AFB, Texas. 141 pp.

Durney, C. H., M. F. Iskander, H. Massoudi, and C. C. Johnson. 1979. An Empirical Formula for Broad-Band SAR Calculations of Prolate Spheroidal Models of Humans and Animals. IEEE Trans. Microwave Theory Techniques, MTT-27(8):758-763.

Durney, C. H., M. F. Iskander, H. Massoudi, S. J. Allen, and J. C. Mitchell. 1980. Radiofrequency Radiation Dosimetry Handbook, 3rd ed. Report SAM-TR-80-32, USAF School of Aerospace Medicine, Brooks AFB, Texas. 136 pp.

Dutta, S. K., W. H. Nelson, C. F. Blackman, and D. J. Brusick. 1979a. Lack of Microbial Genetic Response to 2.45-GHz CW and 8.5 to 9.6-GHz Pulsed Microwaves. J. Microwave Power, 14:275-280.

Dutta, S. K., M. A. Hossain, H. S. Ho, and C. F. Blackman. 1979b. Effects of 8.6-GHz Pulsed Electromagnetic Radiation on an Escherichia coli Repair-Deficient Mutant. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. Edmonton, Canada. pp. 76-95.

Dutta, S. K., W. H. Nelson, C. F. Blackman, and D. J. Brusick. 1980. Cellular Effects in Microbial Tester Strains Caused by Exposure to Microwaves or Elevated Temperatures. J. Environ. Pathol. Toxicol., 3:195-206.

Dwyer, M. J., and D. B. Leeper. 1978. A Current Literature Report on the Carcinogenic Properties of Ionizing and Non-Ionizing Radiation. II. Microwave and Radiofrequency Radiation. DHEW Publication (NIOSH) No. 78-134. 28 pp.

Edelwejn, Z. 1968. Attempt at Evaluation of the Functional State of Brain Synapses in Rabbits Exposed Chronically to the Action of Microwaves. Acta Physiol. Polon., 19:791-799.

Edwards, M. J. 1974. The Effects of Hyperthermia on Pregnancy and Prenatal Development. In: Experimental Embryology and Teratology, Vol. 1, D. H. M. Woollam and G. M. Morriss, eds. Paul Elek, London, England. pp. 90-133.

Edwards, W. P., and H. S. Ho. 1975. RF Cavity Irradiation Dosimetry. IEEE Trans. Microwave Theory Techniques, MTT-23(3):311-313.

Elder, J. A., and J. S. Ali. 1975. The Effect of Microwaves (2450 MHz) on Isolated Rat Liver Mitochondria. Ann. N.Y. Acad. Sci., 247:251-262.

Elder, J. A., J. S. Ali, M. D. Long, and G. E. Anderson. 1976. A Coaxial Air Line Microwave Exposure System: Respiratory Activity of Mitochondria Irradiated at 2-4 GHz. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 352-365.

Elizondo, R. S. 1973. Local Control of Eccrine Sweat Gland Function. Fed. Proc., 32:1583-1587.

Ellis, F. P., H. M. Ferres, A. R. Lind, and P. S. B. Newling. 1960. The Upper Limits of Tolerance of Environmental Stress. In: Physiological Responses to Hot Environments. Spec. Report, Series No. 298. Med. Res. Council, London. pp. 158-179.

Ely, T. S., D. E. Goldman, and J. Z. Hearon. 1964. Heating Characteristics of Laboratory Animals Exposed to Ten-Centimeter Microwaves. IEEE Trans. Biomed. Eng., 11:123-137.

Emery, A. F., R. E. Short, A. W. Guy, and K. K. Kraning. 1976. The Numerical Thermal Simulation of the Human Body When Undergoing Exercise or Nonionizing Electromagnetic Irradiation. Trans. ASME, J. Heat Transfer, 98:284-291.

Epidemiology Work Group. 1981. Guidelines for Documentation of Epidemiologic Studies. Am. J. Epidemiol., 114:609-613.

Fahim, M. S., Z. Fahim, R. Der, D. G. Hall, and J. Harman. 1975. Heat in Male Contraception (Hot Water 60° C, Infrared, Microwave, and Ultrasound). Contraception, 11(5):549-562.

Fermi, E., J. R. Pasta, and S. Ulam. 1965. Studies of Non Linear Problems. In: Collected Works of Enrico Fermi, Vol. II. University of Chicago Press, Chicago, Illinois. pp. 978-988.

Ferri, E. S., and G. J. Hagan. 1976. Chronic Low-Level Exposure of Rabbits to Microwaves. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010. pp. 129-142.

Flynn, R.J. 1968. Exencephalia: Its Occurrence in Untreated Mice. Science, 160:898-899.

Folk, G. E., Jr. 1974. Textbook of Environmental Physiology, 2nd ed. Lea and Febiger, Philadelphia, Pennsylvania. 466 pp.

Foster, K. R., and E. D. Finch. 1974. Microwave Hearing: Evidence for Thermoacoustic Auditory Stimulation by Pulsed Microwaves. Science, 185:256-258.

Frazer, J. W., J. H. Merritt, S. J. Allen, R. H. Hartzell, J. A. Ratliff, A. F. Chamness, R. E. Detwiler, and T. McLellan. 1976. Thermal Responses to High Frequency Electromagnetic Radiation Fields. Doc. No. SAM-TR-76-20, USAF School of Aerospace Med., Brooks Air Force Base, Texas. 16 pp.

Frey, A. H. 1961. Auditory System Response to Radio Frequency Energy. Aerospace Med., 32:1140-1142.

Frey, A. H. 1962. Human Auditory System Response to Modulated Electromagnetic Energy. J. Appl. Physiol., 17:689-692.

Frey, A. H. 1963. Some Effects on Human Subjects of Ultra-High-Frequency Radiation. Am. J. Med. Electron., 2:28-31.

Frey, A. H. 1967. Brain Stem Evoked Responses Associated with Low-Intensity Pulsed UHF Energy. J. Appl. Physiol., 23:984-988.

Frey, A. W., and E. Coren. 1979. Holographic Assessment of Hypothesized Microwave Hearing Mechanism. Science, 206:232-234.

Frey, A. H., and S. R. Feld. 1975. Avoidance by Rats of Illumination with Low Power Nonionizing Electromagnetic Energy. J. Comp. Physiol. Psychol., 89:183-188.

Frey, A. H., and R. Messenger. 1973. Human Perception of Illumination with Pulsed Ultrahigh-Frequency Electromagnetic Energy. Science, 181:356-358.

Frey, A. H., and E. Seifert. 1968. Pulse Modulated UHF Illumination of the Heart Associated with Change in Heart Rate. Life Sci., 7:505-512.

Frey, A. H., S. R. Feld, and B. Frey. 1975. Neural Function and Behavior: Defining the Relationship. Ann. N.Y. Acad. Sci., 247:433-439.

Friedman, H. L. 1981. Are Chronic Exposure to Microwaves and Polycythemia Associated? New England J. Med., 304:357-358.

Froëhlich, J. P. 1969. Information Transmittal and Communicating Systems. Holt, Rinehart, and Winston, New York, New York. 274 pp.

Fröhlich, H. 1968. Long Range Coherence and Energy Storage in Biological Systems. Int. J. Quant. Chem., 2:641-649.

Fröhlich, H. 1975. The Extraordinary Dielectric Properties of Biological Materials and the Action of Enzymes. Proc. Natl. Acad. Sci. USA, 72:4211-4215.

Gage, M. I. 1979a. Behavior in Rats after Exposures to Various Power Densities of 2450 MHz Microwaves. Neurobehav. Toxicol., 1:137-143.

Gage, M. I. 1979b. Microwave Irradiation and Ambient Temperature Interact to Alter Rat Behavior Following Overnight Exposure. J. Microwave Power, 14:389-398.

Gage, M. I., E. Berman, and J. B. Kinn. 1979. Videotape Observation of Rats and Mice During an Exposure to 2450 MHz Microwave Radiation. Radio Sci., 14(6S):227-232.

Gale, C. C. 1973. Neuroendocrine Aspects of Thermoregulation. Annu. Rev. Physiol., 35:391-430.

Gandhi, O. P. 1980. State of the Knowledge for Electromagnetic Absorbed Dose in Man and Animals. Proc. IEEE, 68(1):24-32.

Gandhi, O. P., E. L. Hunt, and J. A. D'Andrea. 1977. Deposition of Electromagnetic Energy in Animals and in Models of Man with and without Grounding and Reflector Effects. Radio Sci., 12(6S):39-47.

Gandhi, O. P., M. J. Hagmann, and J. A. D'Andrea. 1979. Part-Body and Multi-Body Effects on Absorption of Radio-Frequency Electromagnetic Energy by Animals and by Models of Man. Radio Sci., 14(6S):15-21.

Gavalas-Medici, R., and S. R. Day-Magdaleno. 1976. Extremely Low Frequency, Weak Electric Fields Affect Schedule-Controlled Behavior of Monkeys. Nature, 261:256-258.

Gersten, J. W., K. G. Wakim, J. F. Herrick, and F. H. Krusen. 1949. The Effect of Microwave Diathermy on the Peripheral Circulation and on Tissue Temperature in Man. Arch. Physical Med., 30:7-25.

Ginoza, W., and R. C. Miller. 1965. Kinetics of X-Ray and Heat Inactivation of ϕX174 RF-DNA. Proc. Natl. Acad. Sci. USA, 54:551-558.

Ginoza, W., C. J. Hoelle, K. B. Vessey, and C. Carmack. 1964. Mechanisms of Inactivation of Single-Stranded Virus Nucleic Acids by Heat. Nature, 203(4945):606-609.

Ginzburg, V. L. 1968. The Problem of High Temperature Superconductivity. Contemp. Phys., 9:355-374.

Goldblith, S. A., and D. I. C. Wang. 1967. Effect of Microwaves on Escherichia coli and Bacillus subtilus. Appl. Microbiol., 15:1371-1375.

Goldstein, L., and Z. Sisko. 1974. A Quantitative Electroencephalographic Study of the Acute Effects of X-Band Microwaves in Rabbits. In: Biologic Effects and Health Hazards of Microwave Radiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess, and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 128-133.

Gordon, C. J. 1982a. Effects of Ambient Temperature and Exposure to 2450-MHz Microwave Radiation on Evaporative Heat Loss in the Mouse. J. Microwave Power, 17:145-150.

Gordon, C. J. 1982b. Open-Loop Gain of Evaporative Heat Loss During Radiant Heat Exposure in the Mouse. Am. J. Physiol., 242:R275-R279.

Gordon, Z. V. 1970. Biological Effect of Microwaves in Occupational Hygiene. Israel Program for Scientific Translations, Jerusalem, Israel. NASA TT F-633, TT 70-50087; NTIS N71-14632. 101 pp.

Gournay, L. S. 1966. Conversion of Electromagnetic to Acoustic Energy by Surface Heating. J. Acous. Soc. Amer., 40:1322-1330.

Grant, E. H., S. E. Keefe, and S. Takashima. 1968. The Dielectric Behavior of Aqueous Solutions of Bovine Serum Albumin from Radiowave to Microwave Frequencies. J. Phys. Chem., 72:4373-4380.

Grant, E. H., R. J. Sheppard, and G. P. South. 1978. Dielectric Behaviour of Biological Molecules in Solution, Oxford University Press, Oxford, England. 237 pp.

Greene, F. M. 1975a. Development of Electric and Magnetic Near-Field Probes. NBS Technical Note 658 (COM-75-50161), U.S. Department of Commerce, National Bureau of Standards, Boulder, Colorado. 47 pp.

Greene, F. M. 1975b. Development of Magnetic Near-Field Probes. HEW Publication (NIOSH) 75-127, U.S. Department of Health, Education, and Welfare, Public Health Service, Cincinnati, Ohio. 28 pp.

Greene, F. M. 1976. Development of an RF Near-Field Exposure Synthesizer (10 to 40 MHz). HEW Publication (NIOSH) 76-160. U.S. Department of Health, Education, and Welfare, Public Health Service, Cincinnati, Ohio. 36 pp.

Grell, R. F. 1971. Heat-Induced Exchange in the Fourth Chromosome of Diploid Females of Drosophila Melanogaster. Genetics, 69:523-527.

Grundler, W., and F. Keilmann. 1980. Frequency Fine-Tuning Studies of Microwave Influenced Yeast Growth (Abstract). Presented at the International Symposium on Electromagnetic Waves and Biology, Jouy-en-Josas, France, June 30-July 4, 1980. p. 4.

Grundler, W., F. Keilmann, and H. Fröhlich. 1977. Resonant Growth Rate Response of Yeast Cells Irradiated by Weak Microwaves. Phys. Lett., 62A:463-466.

Guillet, R., and S. M. Michaelson. 1977. The Effect of Repeated Microwave Exposure on Neonatal Rats. Radio Sci., 12(6S):125-129.

Gunn, S. A., T. C. Gould, and W. A. D. Anderson. 1961. The Effect of Microwave Radiation on Morphology and Function of Rat Testis. Lab. Invest., 10(2):301-314.

Guy, A. W. 1971. Analyses of Electromagnetic Fields Induced in Biological Tissues by Thermographic Studies on Equivalent Phantom Models. IEEE Trans. Microwave Theory Techniques, MTT-19(2):205-214.

Guy, A. W. 1975. Correspondence on D. R. Justesen's "Prescriptive Grammar for the Radiobiology of Nonionizing Radiation." J. Microwave Power, 10(4):358-359.

Guy, A. W. 1977. A Method for Exposing Cell Cultures to Electromagnetic Fields under Controlled Conditions of Temperature and Field Strength. Radio Sci., 12(6S):87-96.

Guy, A. W. 1979. Miniature Anechoic Chamber for Chronic Exposure of Small Animals to Plane-Wave Microwave Fields. J. Microwave Power, 14(4):327-338.

Guy, A. W., and C. K. Chou. 1976. System for Quantitative Chronic Exposure of a Population of Rodents to UHF Fields. In: Biological Effects of Electromagnetic Waves, Vol. II, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8011. pp. 389-410.

Guy, A. W., and S. F. Korbel. 1972. Dosimetry Studies of a UHF Cavity Exposure Chamber for Rodents. Summaries of Presented Papers for 1972 Microwave Power Symposium, Ottawa, Canada. Int. Microwave Power Institute, Edmonton, Alberta. pp. 180-193.

Guy, A. W., C. C. Johnson, J. C. Lin, A. F. Emery, and K. K. Kraning. 1973. Electromagnetic Power Deposition in Man Exposed to High Frequency Fields and the Associated Thermal and Physiologic Consequences. Doc. No. SAM-TR-73-13 (NTIS AD-776 821), USAF School of Aerospace Medicine, Brooks Air Force Base, Texas. 71 pp.

Guy, A. W., J. C. Lin, P. O. Kramar, and A. F. Emery. 1974. Quantitation of Microwave Radiation Effects on the Eyes of Rabbits at 2450 MHz and 918 MHz. Office of Naval Research, Arlington, Virginia. NTIS AD-A007 521. 39 pp.

Guy, A. W., J. C. Lin, P. O. Kramar, and A. F. Emery. 1975a. Effect of 2450-MHz Radiation on the Rabbit Eye. IEEE Trans. Microwave Theory Techniques, MTT 23:492-498.

Guy, A. W., C. K. Chou, J. C. Lin, and D. Christensen. 1975b. Microwave-Induced Acoustic Effects in Mammalian Auditory Systems and Physical Materials. Ann. N.Y. Acad. Sci., 247:194-215.

Guy, A. W., M. D. Webb, and J. A. McDougall. 1975c. A New Technique for Measuring Power Deposition Patterns in Phantoms Exposed to EM Fields of Arbitrary Polarization: Example the Microwave Oven. Microwave Power Symposium Proc., Waterloo, Ontario, Canada. pp. 36-47.

Guy, A. W., M. D. Webb, and C. C. Sorenson. 1976. Determination of Power Absorption in Man Exposed to High Frequency Electromagnetic Fields by Thermographic Measurements on Scale Models. IEEE Trans. Biomed. Eng., BME-23(5):361-371.

Guy, A. W., M. D. Webb, and J. A. McDougal. 1977. RF Radiation Absorption Patterns: Human and Animal Modeling Data. HEW Publication (NIOSH) 77-183, U.S. Department of Health, Education, and Welfare, Public Health Service, Cincinnati, Ohio. 67 pp.

Guy, A. W., M. D. Webb, A. F. Emery, and C. K. Chou. 1978. Determination of the Average SAR and SAR Patterns in Man and Simplified Models of Man and Animals Exposed to Radiation Fields from 50-2450 MHz and the Thermal Consequences (Abstract). Symposium on the Biological Effects of Electromagnetic Waves, XIX General Assembly, International Union of Radio Science, Helsinki, Finland. p. 13.

Guy, A. W., J. Wallace, and J. A. McDougall. 1979. Circularly Polarized 2450-MHz Waveguide System for Chronic Exposure of Small Animals to Microwaves. Radio Sci., 14(6S):63-74.

Guy, A. W., C. K. Chou, R. B. Johnson, and L. L. Kunz. 1980. Study of Effects of Long-Term, Low-Level RF Exposure on Rats: A Plan. Proc. IEEE, 68(1):92-97.

Hagan, G. J., and R. L. Carpenter. 1976. Relative Cataractogenic Potencies of Two Microwave Frequencies (2.45 and 10 GHz). In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010. pp. 143-155.

Hagmann, M. J., and O. P. Gandhi. 1979. Numerical Calculation of Electromagnetic Energy Deposition in Models of Man with Grounding and Reflector Effects. Radio Sci., 14(6S):23-29.

Hagmann, M. J., O. P. Gandhi, and C. H. Durney. 1979a. Numerical Calculation of Electromagnetic Energy Deposition for a Realistic Model of Man. IEEE Trans. Microwave Theory Techniques, MTT-27(9):804-809.

Hagmann, M. J., O. P. Gandhi, J. A. D'Andrea, and I. Chatterjee. 1979b. Head Resonance: Numerical Solutions and Experimental Results. IEEE Trans. Microwave Theory and Techniques, MTT-27(9):809-813.

Hammel, H. T. 1968. Regulation of Internal Body Temperature. Annu. Rev. Physiol., 30:641-710.

Hamnerius, Y., H. Olofsson, A. Rasmuson, and B. Rasmuson. 1979. A Negative Test for Mutagenic Action of Microwave Radiation in Drosophila melanogaster. Mutat. Res., 68:217-223.

Hamrick, P. E. 1973. Thermal Denaturation of DNA Exposed to 2450 MHz CW Microwave Radiation. Radiat. Res., 56:400-404.

Hamrick, P. E., and B. T. Butler. 1973. Exposure of Bacteria to 2450 MHz Microwave Radiation. J. Microwave Power, 8:227-233.

Hamrick, P. E., and S. S. Fox. 1977. Rat Lymphocytes in Cell Culture Exposed to 2450 MHz (CW) Microwave Radiation. J. Microwave Power, 12:125-132.

Hamrick, P. E., and D. I. McRee. 1975. Exposure of the Japanese Quail Embryo to 2.45-GHz Microwave Radiation During the Second Day of Development. J. Microwave Power, 10:211-221.

Hamrick, P., and D. I. McRee. 1980. The Effect of 2450 MHz Microwave Irradiation on the Heart Rate of Embryonic Quail. Health Phys., 38:261-268.

Hamrick, P. E., and J. G. Zinkl. 1975. Exposure of Rabbit Erythrocytes to Microwave Radiation. Radiat. Res., 62:164-168.

Hamrick, P. E., D. I. McRee, P. Thaxton, and C. R. Parkhurst. 1977. Humoral Immunity of Japanese Quail Subjected to Microwave Radiation During Embryogeny. Health Phys., 33:23-33.

Hardy, J. D. 1949. Heat Transfer. In: Physiology of Heat Regulation, L. H. Newburgh, ed. W. B. Saunders, Philadelphia, Pennsylvania. pp. 78-108.

Harper, H. A. 1975. Review of Physiological Chemistry, 15th ed. Lange Medical Publications, Los Altos, California. pp. 446-504.

Harrison, G. H., J. E. Robinson, D. McCulloch, and A. Y. Cheung. 1980. Comparison of Hyperthermal Cellular Survival in the Presence or Absence of 2.45 GHz Microwave Radiation. In: Ondes Electromagnetiques et Biologie, A. J. Berteaud and B. Servantie, eds. Paris, France. pp. 41-45.

Heller, J. H. 1970. Cellular Effects of Microwave Radiation. In: Biological Effects and Health Implications of Microwave Radiation, S. F. Cleary, ed. HEW Publication BRH/DBE 70-2. Bureau of Radiological Health, Rockville, Maryland. pp. 116-121.

Henderson, H. M., K. Hergenroeder, and S. S. Stuchly. 1975. Effect of 2450 MHz Microwave Radiation on Horseradish Peroxidase. J. Microwave Power, 10:27-35.

Hendler, E. 1968. Cutaneous Receptor Response to Microwave Irradiation. In: Thermal Problems in Aerospace Medicine, J. D. Hardy, ed. Technivision Services, Maidenhead, England. pp. 149-161.

Hendler, E., J. D. Hardy, and D. Murgatroyd. 1963. Skin Heating and Temperature Sensation Produced by Infra Red and Microwave Irradiation. In: Temperature: Its Measurement and Control in Science and Industry, Part 3, Biology and Medicine, C. M. Herzfeld, ed. Reinhold, New York, New York. pp. 211-230.

Hensel, H. 1973. Neural Processes in Thermoregulation. Physiol. Rev., 53:948-1017.

Heynick, L. N., P. Polson, and A. Karp. 1977. A Microwave Exposure System for Primates. Radio Sci., 12:103-110.

Hinde, R. A. 1970. Animal Behavior: A Synthesis of Ethology and Comparative Psychology. Second Ed. McGraw-Hill, New York, New York. 876 pp.

Hizal, A., and Y. K. Baykal. 1978. Heat Potential Distribution in an Inhomogeneous Spherical Model of a Cranial Structure Exposed to Microwaves Due to Loop or Dipole Antennae. IEEE Trans. Microwave Theory Techniques, MTT 26(8):607-612.

Hjeresen, D. L., S. R. Doctor, and R. L. Sheldon. 1979. Shuttlebox Side Preference as Mediated by Pulsed Microwave and Conventional Auditory Cues. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. Ottawa, Canada. pp. 194-214.

Ho, H. S. 1975. Dose Rate Distribution in Triple-Layered Dielectric Cylinder with Irregular Cross Section Irradiated by Plane Wave Sources. J. Microwave Power, 10(4):421-432.

Ho, H. S. 1978. Effect of Plexiglas Animal Holders on Microwave Energy Absorption. IEEE Trans. Biomed. Eng., BME-25(5):474-476.

Ho, H. S., and W. P. Edwards. 1977a. Dose Rate and Oxygen Consumption Rate in Mice Confined in a Small Holder During Exposure to 2450 MHz Radiation. Radiat. Environ. Biophys., 14:251-256.

Ho, H. S., and W. P. Edwards. 1977b. Oxygen-Consumption Rate of Mice under Differing Dose Rates of Microwave Radiation. Radio Sci., 12(6S):131-138.

Ho, H. S., and W. P. Edwards. 1979. The Effect of Environmental Temperature and Average Dose Rate of Microwave Radiation on the Oxygen-Consumption Rate of Mice. Radiat. Environ. Biophys. 16:325-338.

Ho, H. S., and M. McManaway. 1977. Heat-Dissipation Rate of Mice after Microwave Irradiation. J. Microwave Power, 12:93-100.

Ho, H. S., E. I. Ginns, and C. L. Christman. 1973. Environmentally Controlled Waveguide Irradiation Facility. IEEE Trans. Microwave Theory Techniques, MTT-21:837-840.

Ho, H. S., M. R. Foster, and M. L. Swicord. 1976. Microwave Irradiation Apparatus Design and Dosimetry. In: Biological Effects of Electromagnetic Waves, Vol. II, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8011. pp. 423-434.

Hollaender, A. 1971. Chemical Mutagens, Principles and Methods for Their Detection. Vols. 1, 2, and 3. Plenum Press, New York, New York.

Honig, W. K., and J. E. R. Staddon, eds. 1977. Handbook of Operant Behavior. Prentice-Hall, Englewood Cliffs, New Jersey. 689 pp.

Huang, A. T., and N. G. Mold. 1980. Immunologic and Hematopoietic Alterations by 2450-MHz Electromagnetic Radiation. Bioelectromagnetics, 1:77-87.

Huang, A. T., M. E. Engle, J. A. Elder, J. B. Kinn, and T. R. Ward. 1977. The Effect of Microwave Radiation (2450 MHz) on the Morphology and Chromosomes of Lymphocytes. Radio Sci., 12(6S):173-177.

Hunt, E. L., and R. D. Phillips. 1972. Absolute Physical Dosimetry for Whole Animal Experiments. Digest of Papers of the Microwave Dosimetry Workshop, Atlanta, Georgia. pp. 74-77.

Hunt, E. L., N. W. King, and R. D. Phillips. 1975. Behavioral Effects of Pulsed Microwave Radiation. Ann. N.Y. Acad. Sci., 247:440-453.

IEEE Microwave Theory and Techniques Society. 1980. Symposium on Electromagnetic Dosimetric Imagery, Washington, D.C. Institute of Electrical and Electronic Engineers.

Illinger, K. H. 1970. Molecular Mechanisms for Microwave Absorption in Biological Systems. In: Biological Effects and Health Implications of Microwave Radiation, S. F. Cleary, ed. BRH/DBE 70-2. Bureau of Radiological Health, Rockville, Maryland. pp. 112-115.

Illinger, K. H. 1982. Spectroscopic Properties of In Vivo Biological Systems: Boson Radiative Equilibrium with Steady-State Nonequilibrium Molecular Systems. Bioelectromagnetics, 3:9-16.

Iskander, M. F., C. H. Durney, H. Massoudi, and C. C. Johnson. 1979. Approximate Calculation of SAR for Planewave Irradiation of Man Model Near a Ground Plane. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. International Microwave Power Institute, Edmonton, Alberta, Canada. pp. 304-323.

Iskander, M. F., P. W. Barber, C. H. Durney, and H. Massoudi. 1980. Irradiation of Prolate Spheroidal Models of Humans in the Near Field of a Short Electric Dipole. IEEE Trans. Microwave Theory Techniques, MTT-28(7):801-807.

Ismailov, E. Sh. 1971. Mechanism of Effects of Microwaves on Erythrocyte Permeability for Potassium and Sodium Ions. Biol. Nauki, 3:58-60 (English trans.: JPRS 72606, Jan. 12, 1979, pp. 38-41).

Ismailov, E. Sh. 1977. Infrared Spectra of Erythrocyte Ghosts in the Region of the Amide I and Amide II Bands on Microwave Irradiation. Biophysics, 21:961-963 (trans. of Biofizika 21:940-942, 1976).

Ismailov, E. Sh. 1978. Effect of Ultrahigh Frequency Electromagnetic Radiation on the Electrophoretic Mobility of Erythrocytes. Biophysics, 22:510-516 (trans. of Biofizika 22:493-498, 1977).

Jensh, R. P. 1979. Biological Effects of 6 GHz Microwave Irradiation. Final Report, GTEL Grant 08000-1106. 131 pp.

Jensh, R. P. 1980. Behavioural Teratology: Application in Low Dose Chronic Microwave Irradiation Studies. In: Neural and Behavioural Teratology (Vol. 4, Advances in the Study of Birth Defects), T. V. N. Persaud, ed. University Park Press, Baltimore, Maryland. pp. 135-162.

Jensh, R. P., J. Ludlow, W. H. Vogel, T. McHugh, I. Weinberg, and R. L. Brent. 1979. Studies Concerning the Effects of Non-Thermal Protracted Prenatal 915 MHz Microwave Radiation on Prenatal and Postnatal Development in the Rat. XIV Internat. Symp. on the Applications of Microwave Energy, IMPI, Paris, France. pp. 99-101.

Johansen, K. 1963. Cardiovascular Dynamics in the Amphibian, Amphiuma tridactylum Cuvier. Acta Physiol. Scand., 60:1-82.

Johnson, C. C. 1975. Recommendations for Specifying EM Wave Irradiation Conditions in Bioeffects Research. J. Microwave Power, 10(3):249-250.

Johnson, C. C., and A. W. Guy. 1972. Nonionizing Electromagnetic Wave Effects in Biological Materials and Systems. Proc. IEEE, 60:692-718.

Johnson, R. B., D. E. Meyers, A. W. Guy, R. H. Lovely, and R. Galambos. 1976. Discriminative Control of Appetitive Behavior by Pulsed Microwave Radiation in Rats. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 238-247.

Johnson, R. B., S. Mizumori, and R. H. Lovely. 1978. Adult Behavioral Deficit in Rats Exposed Prenatally to 918-MHz Microwaves. In: Developmental Toxicology of Energy-Related Pollutants. D. D. Mahlum, M. R. Sikov, P. L. Hackett, and F. D. Andrew, eds. DOE Symposium Series 47, Washington, D.C. pp. 281-299.

Joines, W. T., and C. F. Blackman. 1980. Power Density, Field Intensity, and Carrier Frequency Determinants of RF-Energy-Induced Calcium Ion Efflux from Brain Tissue. Bioelectromagnetics 1:271-275.

Justesen, D. R. 1975. Toward a Prescriptive Grammar for the Radiobiology of Non-Ionising Radiations: Quantities, Definitions, and Units of Absorbed Electromagnetic Energy--An Essay. J. Microwave Power, 10(4):343-356.

Justesen, D. R. 1980. Microwave Irradiation and Blood-Brain Barrier. Proc. IEEE, 68:60-67.

Justesen, D. R., D. M. Levinson, R. L. Clarke, and N. W. King. 1971. A Microwave Oven for Behavioural and Biological Research: Electrical and Structural Modifications, Calorimetric, Dosimetry, and Functional Evaluation. J. Microwave Power, 6:237-258.

Justesen, D. R., D. M. Levinson, and L. R. Justesen. 1974. Psychogenic Stressors are Potent Mediators of the Thermal Response to Microwave Irradiation. In: Biologic Effects and Health Hazards of Microwave Irradiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess, and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 134-140.

Justesen, D. R., H. A. Ragan, L. E. Rogers, A. W. Guy, D. L. Hjeresen, W. T. Hinds, and R. D. Phillips. 1978. Compilation and Assessment of Microwave Bioeffects. A Selective Review of the Literature on Biological Effects of Microwaves in Relation to the Satellite Power System (SPS). PNL-2634, U.S. Department of Energy. Washington, D.C. 65 pp.

Kaczmarek, L. K., and W. R. Adey. 1973. The Efflux of $^{45}Ca^{2+}$ and [^{3}H]γ-Aminobutyric Acid from Cat Cerebral Cortex. Brain Res., 63:331-342.

Kantor, G., and T. C. Cetas. 1977. A Comparative Heating-Pattern Study of Direct-Contact Applicators in Microwave Diathermy. Radio Sci., 12(6S):111-120.

Kaplan, J. N. 1981. Study of the Lethal Effects of Microwaves in the Developing Squirrel Monkey. Final Report for Contract No. 68-02-3210, U.S. Environmental Protection Agency, Health Effects Research Laboratory, Research Triangle Park, North Carolina. 54 pp.

Kaplan, I. T., W. Metlay, M. M. Zaret, L. Birenbaum, and S. W. Rosenthal. 1971. Absence of Heart-Rate Effects in Rabbits During Low-Level Microwave Irradiation. IEEE Trans. Microwave Theory Techniques, MTT-19:168-173.

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage. 1982. Biological and Behavioral Effects of Prenatal and Postnatal Exposure to 2450-MHz Electromagnetic Radiation in the Squirrel Monkey. Radio Sci.: 17(5S):135S-144S.

Keilmann, F. 1978. Nonthermal Microwave Resonances in Living Cells. In: Coherence in Spectroscopy and Modern Physics, F. T. Arecchi, R. Bonifacio, and M. O. Scully, eds. NATO Advanced Study Institute Series: Series B, Physics, Vol. 37. Plenum Publishing Corp., New York, New York. pp. 347-360.

Kerslake, D. McK., and J. L. Waddell. 1958. The Heat Exchange of Wet Skin. J. Physiol., 141:156-163.

King, N. W., D. R. Justesen, and A. D. Simpson. 1970. The Photo-Lickerandum: A Device for Detecting the Licking Response with Capability for Near-Instantaneous Programming of Variable Quantum Reinforcement. Behav. Res. Meth. Instrument., 2:125-129.

King, N. W., D. R. Justesen, and R. L. Clarke. 1971. Behavioral Sensitivity to Microwave Irradiation. Science, 172:398-401.

Kinn, J. B. 1977. Whole-Body Dosimetry of Microwave Radiation in Small Animals: The Effect of Body Mass and Exposure Geometry. Radio Sci., 12(6S):61-64.

Kirkwood, J. G., and J. B. Schumaker. 1952. The Influence of Dipole Moment Fluctuations on the Dielectric Increment of Proteins in Solution. Proc. Nat. Acad. Sci., 38:855-862.

Kitsovskaya, I. A. 1964. The Effect of Centimeter Waves of Different Intensities on the Blood and Hemopoietic Organs of White Rats. Gigiena Truda Prof Zabolev, 8:14-25.

Kleiber, M. 1961. The Fire of Life. An Introduction to Animal Energetics, 1st ed. John Wiley, New York, New York.

Kleiber, M. 1975. The Fire of Life. An Introduction to Animal Energetics, rev. ed. R. E. Krieger, Huntington, New York. 453 pp.

Kling, J. W., and L. A. Riggs, eds. 1971. Woodworth and Schlosberg's Experimental Psychology, 3rd ed. Holt Rinehart and Winston, New York, New York. 1279 pp.

Konorski, J. 1967. Integrative Activity of the Brain. The University of Chicago Press, Chicago, Illinois. 531 pp.

Kramar, P. O., A. F. Emery, A. W. Guy, and J. C. Lin. 1975. The Ocular Effects of Microwaves on Hypothermic Rabbits: A Study of Microwave Cataractogenic Mechanisms. Ann. N.Y. Acad. Sci., 247:155-165.

Kramar, P. O., C. Harris, A. W. Guy, and A. F. Emery. 1976. Mechanism of Microwave Cataractogenesis in Rabbits. In: Biological Effects of Electromagnetic Waves, Vol. 1, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010. pp. 49-60.

Kritikos, H. N., and H. P. Schwan. 1975. The Distribution of Heating Potential Inside Lossy Spheres. IEEE Trans. Biomed. Eng., BME-22(6):457-463.

Krupp, J. H. 1977. Thermal Response in Macaca Mulatta Exposed to 15- and 20-MHz Radiofrequency Radiation. Report No. SAM-TR-77-16, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas. 10 pp.

Lacy, K. K., J. M. Desesso, and J. M. Lary. 1980a. A Comparison of the Teratogenic Effects of Radiofrequency Radiation and Hyperthermia: Gross Evaluation (Abstract). Teratology, 21:51A.

Lacy, K. K., J. M. Desesso, T. W. Sadler, and J. M. Lary. 1980b. A Comparison of the Teratogenic Effects of Radiofrequency Radiation and Hyperthermia: Light Microscopic Evaluation (Abstract). Teratology, 21:52A.

Lancranjan, I., M. Maicanescu, E. Rafaila, I. Klepsch, and H. I. Popescu. 1975. Gonadic Function in Workmen with Long-Term Exposure to Microwaves. Health Phys., 29:381-383.

Lappenbusch, W. L., L. J. Gillespie, W. M. Leach, and G. E. Anderson. 1973. Effect of 2450-MHz Microwaves on the Radiation Response of X-Irradiated Chinese Hamsters. Radiat. Res., 54:294-303.

Lary, J. M., D. L. Conover, E. D. Foley, and P. L. Hanser. 1979. Teratogenicity of 27.12 MHz Radiofrequency Radiation in Rats (Abstract). Teratology, 19:36A.

Lary, J. M., D. L. Conover, E. D. Foley, and P. L. Hanser. 1980. Teratogenicity of 27.12 MHz Radiofrequency Radiation in Rats (Abstract). Bioelectromagnetics Symposium, Seattle, Washington. p. 402.

Lary, J. M., D. L. Conover, E. D. Foley, and P. L. Hanser. 1982. Teratogenic Effects of 27.12 MHz Radiofrequency Radiation in Rats. Teratology, 26:299-309.

Lebovitz, R. M., and R. L. Seaman. 1977. Microwave Hearing: The Response of Single Auditory Neurons in the Cat to Pulsed Microwave Radiation. Radio Sci. 12(6S):229-236.

Leden, U. M., J. F. Herrick, K. G. Wakim, and F. H. Krusen. 1947. Preliminary Studies on the Heating and Circulating Effects of Microwaves-"Radar." Brit. J. Phys. Med., Nov/Dec:177-184.

Lehninger, A. L. 1975. Biochemistry, 2nd ed. Worth Publishers, Inc., New York, New York. pp. 143-144, 875-876.

LeVeen, H. H., S. Wapnick, V. Piccone, G. Falk, and N. Ahmed. 1976. Tumor Eradication by Radiofrequency Therapy. Response in 21 Patients. J. Am. Med. Ass., 235:2198-2200.

Liburdy, R. P. 1977. Effects of Radio-Frequency Radiation on Inflammation. Radio Sci., 12(6S):179-183.

Liburdy, R. P. 1979. Radiofrequency Radiation Alters the Immune System: Modulation of T- and B-Lymphocyte Levels and Cell-Mediated Immunocompetence by Hyperthermic Radiation. Radiat. Res., 77:34-46.

Liburdy, R. P. 1980. Radiofrequency Radiation Alters the Immune System. II. Modulation of In Vivo Lymphocyte Circulation. Radiat. Res., 83:66-73.

Lilienfeld, A. M., J. Tonascia, S. Tonascia, C. A. Libauer, and G. M. Cauthen. 1978. Foreign Service Health Status Study--Evaluation of Health Status of Foreign Service and Other Employees from Selected Eastern European

Posts. Final Report, Contract No. 6025-619073 (NTIS PB-288163), Dept. of State, Washington, D.C. 436 pp.

Lin, J. C. 1977. Theoretical Calculation of Frequencies and Thresholds of Microwave-Induced Auditory Signals. Radio Sci., 12:237-242.

Lin, J. C. 1978. Microwave Auditory Effects and Applications. Charles C. Thomas, Springfield, Illinois 221 pp.

Lin, J. C., and M. F. Lin. 1980. Studies on Microwave and Blood-Brain Barrier Interaction. Bioelectromagnetics, 1:313-323.

Lin, J. C., and W. D. Peterson, Jr. 1977. Cytological Effects of 2450 MHz CW Microwave Radiation. J. Bioeng., 1:471-478.

Lin, J. C., A. W. Guy, and C. C. Johnson. 1973. Power Deposition in a Spherical Model of Man Exposed to 1-20 MHz Electromagnetic Fields. IEEE Trans. Microwave Theory Techniques, MTT-21(12):791-797.

Lin, J. C., H. I. Bassen, and C. L. Wu. 1977. Perturbation Effect of Animal Restraining Materials on Microwave Exposure. IEEE Trans. Biomed. Eng., BME-24(1):80-83.

Lin, J. C., J. C. Nelson, and M. E. Ekstrom. 1979a. Effects of Repeated Exposure to 148-MHz Radio Waves on Growth and Hematology of Mice. Radio Sci., 14:(6S)173-179.

Lin, J. C., M. J. Ottenbreit, S. Wang, S. Inoue, R. O. Bollinger, and M. Fracassa. 1979b. Microwave Effects on Granulocyte and Macrophage Precursor Cells of Mice _In_ _Vitro_. Radiat. Res., 80:292-302.

Lindahl, T., and B. Nyberg. 1974. Heat-Induced Deamination of Cytosine Residues in Deoxyribonucleic Acid. Biochemistry, 13(16):3405-3410.

Liu, L. M., F. J. Rosenbaum, and W. F. Pickard. 1976. The Insensitivity of Frog Heart Rate to Pulse Modulated Microwave Energy. J. Microwave Power, 11:225-232.

Livingston, G. K., C. C. Johnson, and L. A. Dethlefsen. 1979. Comparative Effects of Water-Bath- and Microwave-Induced Hyperthermia on Survival of Chinese Hamster Ovary (CHO) Cells. Radio Sci., 14(S):117-123.

Lobanova, E. A. 1974. The Use of Conditioned Reflexes to Study Microwave Effects on the Central Nervous System. In: Biologic Effects and Health Hazards of Microwave Radiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess, and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 110-118.

Lords, J. L., C. H. Durney, A. Borg, and C. Tinney. 1973. Bradycardia in Isolated Hearts Induced by Microwave Irradiation. Int. Microwave Symp., Digest of Technical Papers, Report Series G-MTT, Institute of Electrical and Electronics Engineers, New York, New York. pp. 335-336.

Lotz, W. G., and S. M. Michaelson. 1978. Temperature and Corticosterone Relationships in Microwave-Exposed Rats. J. Appl. Physiol., 44:438-445.

Lovely, R. H., D. E. Myers, and A. W. Guy. 1977. Irradiation of Rats by 918-MHz Microwaves at 2.5 mW/cm^2: Delineating the Dose-Response Relationship. Radio Sci., 12(6S):139-146.

Lu, S., R. Bogardus, J. Cohen, J. Jones, E. Kinnen, S. Michaelson, and R. Mayin. 1974. Thermogenetic and Cardiodynamic Regulation in Dogs Cranially Exposed to 2450 MHz (CW) Microwaves. Int. Microwave Symp., Digest of Technical Papers, Institute of Electrical and Electronics Engineers (IEEE Cat. No. 74CH0838-3MTT), New York, New York. pp. 102-103.

Lu, S., N. Lebda, S. M. Michaelson, S. Pettit, and D. Rivera. 1977. Thermal and Endocrinological Effects of Protracted Irradiation of Rats by 2450-MHz Microwaves. Radio Sci., 12:147-156.

Lu, S., N. Lebda, S. Pettit, and S. M. Michaelson. 1981. Microwave-Induced Temperature, Corticosterone, and Thyrotropin Interrelationships. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol., 50:399-405.

Machle, W., and T. F. Hatch. 1947. Heat: Man's Exchanges and Physiological Responses. Physiol. Rev., 27:200-227.

MacLeod, J., and R. S. Hotchkiss. 1941. The Effect of Hyperpyrexia Upon Spermatozoa Counts in Men. Endocrinology, 28:780-784.

Magin, R. L., S. Lu, and S. M. Michaelson. 1977a. Stimulation of Dog Thyroid by Local Application of High Intensity Microwaves. Am. J. Physiol., 233:E363-E368.

Magin, R. L., S. Lu, and S. M. Michaelson. 1977b. Microwave Heating Effect on the Dog Thyroid Gland. IEEE Trans. Biomed. Eng., BME-24:522-529.

Majewska, K. 1968. Investigations on the Effect of Microwaves on the Eye. Pol. Med. J., 7:989-994.

Manikowska, E., J. M. Luciani, B. Servantie, P. Czerski, J. Obrenovitch, and A. Stahl. 1979. Effects of 9.4 GHz Microwave Exposure on Meiosis in Mice. Experientia, 35:388-390.

Marks, J., E. T. Carter, D. G. Scarpelli, and J. Eisen. 1961. Microwave Radiation to the Anterior Mediastinum of the Dog (II). Ohio State Med. J., 1132-1135.

Marmor, J. B., N. Hahn, and G. M. Hahn. 1977. Tumor Cure and Cell Survival after Localized Radiofrequency Heating. Cancer Res., 37:879-883.

Mathur, D. S., M. A. Aman, and K. R. Sarkar. 1980. Induction of Maternal Haploids in Maize Through Heat Treatment of Pollen. Current Sci., 49:744-746.

Mayers, C. P., and J. A. Habeshaw. 1973. Depression of Phagocytosis: A Non-Thermal Effect of Microwave Radiation as a Potential Hazard to Health. Int. J. Radiat. Biol. 24:449-461.

McAfee, R. D., R. Braus, Jr., and J. Fleming, Jr. 1973. The Effect of 2450 MHz Microwave Irradiation on the Growth of Mice. J. Microwave Power, 8:111-116.

McAfee, R. D., A. Longacre, Jr., R. R. Bishop, S. T. Elder, J. G. May, M. G. Holland, and R. Gordon. 1979. Absence of Ocular Pathology after Repeated Exposure of Unanesthetized Monkeys to 9.3 GHz Microwaves. J. Microwave Power, 14:41-44.

McLaughlin, J. R. 1953. A Survey of Possible Health Hazards from Exposure to Microwave Radiation. Hughes Aircraft Corp., Culver City, California.

McLees, B. D., E. D. Finch, and M. L. Albright. 1972. An Examination of Regenerating Hepatic Tissue Subjected to Radio-Frequency Irradiation. J. Appl. Physiol., 32:78-85.

McNiven, D. R., and D. J. Wyper. 1976. Microwave Therapy and Muscle Blood Flow in Man. J. Microwave Power, 11:168-170.

McRee, D. I., and P. E. Hamrick. 1977. Exposure of Japanese Quail Embryos to 2.45-GHz Microwave Radiation During Development. Radiat. Res., 71:355-366.

McRee, D. I., G. K. Livingston, and G. MacNichols. 1978. Incidence of Sister Chromatid Exchange in Bone Marrow Cells of the Mouse Following Microwave Exposure (Abstract). In: Symposium on Electromagnetic Fields in Biological Systems, IEEE/IMPI, Ottawa, Canada. pp. 15-16.

McRee, D. I., R. Faith, E. E. McConnell, and A. W. Guy. 1980a. Long-Term 2450-MHz CW Microwave Irradiation of Rabbits: Evaluation of Hematological and Immunological Effects. J. Microwave Power, 15:45-52.

McRee, D. I., M. Galvin, C. Hall, and M. Lieberman. 1980b. Microwave Effects on Embryonic Cardiac Tissue of Japanese Quail. In: Ondes Electromagnetiques et Biologie, A. J. Berteaud and B. Servantie, eds. Paris, France. pp. 79-84.

Medical World News. 1974. Cut the Vas or Warm the Testes? Med. World News, May 3, pp 15-16.

Merritt, J. H., R. H. Hartzell, and J. W. Frazer. 1976. The Effect of 1.6 GHz Radiation on Neurotransmitters in Discrete Areas of the Rat Brain. Report No. SAM-TR-76-3, USAF School of Aerospace Medicine, Aerospace Medical Division, Brooks Air Force Base, Texas. 11 pp.

Merritt, J. H., A. F. Chamness, R. H. Hartzell, and S. J. Allen. 1977. Orientation Effects on Microwave-Induced Hyperthermia and Neurochemical Correlates. J. Microwave Power, 12:167-172.

Merritt, J. H., A. F. Chamness, and S. J. Allen. 1978. Studies on Blood-Brain Barrier Permeability after Microwave-Radiation. Radiat. Environ. Biophys., 15:367-377.

Michaelson, S. M., R. A. E. Thomson, and J. W. Howland. 1961. Physiologic Aspects of Microwave Irradiation of Mammals. Am. J. Physiol., 201:351-356.

Michaelson, S. M., R. A. E. Thomson, L. T. Odland, and J. W. Howland. 1963. The Influence of Microwaves on Ionizing Radiation Exposure. Aerospace Med., 34:111-115.

Michaelson, S. M., R. A. E. Thompson, M. Y. El Tamami, H. S. Seth, and J. W. Howland. 1964. The Hematologic Effects of Microwave Exposure. Aerospace Med., 35:824-829.

Michaelson, S. M., R. Guillet, and F. W. Heggeness. 1978. Influence of Microwave Exposure on Functional Maturation of the Rat. In: Developmental Toxicology of Energy-Related Pollutants, D. D. Mahlum, M. R. Sikov, P. L. Hackett, and F. D. Andrew, eds. DOE Symposium Series 47, Washington, D.C. pp. 300-316.

Mickey, G. H., and L. Koerting. 1970. Chromosome Breakage in Cultured Chinese Hamster Cells Induced by Radiofrequency Treatment. Environ. Mutagen Soc., 3:25-26.

Mikolajczyk, H. 1976. Microwave-Induced Shifts of Gonadotropic Activity in Anterior Pituitary Gland of Rats. In: Biological Effects of Electromagnetic Waves, C. C. Johnson and M. L. Shore, eds. U.S. DHEW (FDA) 77-8010, Rockville, Maryland. pp. 377-383.

Milham, S., Jr. 1982. Mortality from Leukemia in Workers Exposed to Electrical and Magnetic Fields. New England J. Med., 307:249.

Milroy, W. C., and S. M. Michaelson. 1972. Thyroid Pathophysiology of Microwave Radiation. Aerospace Med., 43:1126-1131.

Miro, L., R. Loubiere, and A. Pfister. 1974. Effects of Microwaves on the Cell Metabolism of the Reticulo-Histocytic System. In: Biological Effects and Health Hazards of Microwave Radiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. T. Suess, and B. Waldeskog, eds. Polish Medical Publication, Warsaw, Poland. pp. 89-97.

Mitchell, D. S., W. G. Switzer, and E. L. Bronaugh. 1977. Hyperactivity and Disruption of Operant Behavior in Rats after Multiple Exposure to Microwave Radiation. Radio Sci., 12(6S):263-271.

Mittler, S. 1976. Failure of 2- and 10-Meter Radio Waves to Induce Genetic Damage in *Drosophila melanogaster*. Environ. Res., 11:326-330.

Mittler, S. 1977. Failure of Chronic Exposure to Nonthermal FM Radio Waves to Mutate *Drosophila*. J. Heredity, 68:257-258.

Mittler, S. 1979. Hyperthermia and Radiation-Induced Dominant Lethals and Chromosome Loss in Female Drosophila melanogaster. J. Heredity, 70:81-82.

Moe, K. E., R. H. Lovely, D. E. Meyers, and A. W. Guy. 1976. Physiological and Behavioral Effects of Chronic Low Level Microwave Radiation in Rats. In: Biological Effects of Electromagnetic Waves, Vol. I., C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 248-256.

Monahan, J. C., and H. S. Ho. 1976. Microwave Induced Avoidance Behavior in the Mouse. In: Biological Effects of Electromagnetic Waves, Vol. I., C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 274-283.

Monahan, J. C., and H. S. Ho. 1977. The Effect of Ambient Temperature on the Reduction of Microwave Energy Absorption by Mice. Radio Sci., 12(6S):257-262.

Monahan, J. C., and W. W. Henton. 1979. The Effect of Psychoactive Drugs on Operant Behavior Induced by Microwave Radiation. Radio Sci., 14(6S):233-238.

Monjan, A. A. 1981. Stress and Immunologic Competence: Studies in Animals. In: Psychoneuroimmunology, R. Ader, ed. Academic Press, New York, New York. pp. 185-228.

Montgomery, L. D. 1972. A Simulation of Heat Transfer in Man Under Immersed Conditions. Doctoral Thesis, UCLA, Los Angeles, California.

Montgomery, L. D. 1974a. A Model of Heat Transfer in Immersed Man. Ann. Biomed. Eng., 2:19-46.

Montgomery, L. D. 1974b. Analytic Model for Assessing the Thermal Performance of Scuba Divers. J. Hydronautics, 8:108-115.

Montgomery, L. D. 1975. Biothermal Simulation of Scuba Divers. Aviat. Space Environ. Med., 46(6):814-818.

Moore, H. A., R. Raymond, M. Fox, and A. G. Galsky. 1979. Low-Intensity Microwave Radiation and the Virulence of Agrobacterium tumefaciens Strain B6. Appl. Environ. Microbiol., 37: 127-130.

Morishima, H. O., B. Glaser, W. H. Niemann, and L. S. James. 1975. Increased Uterine Activity and Fetal Deterioration During Maternal Hyperthermia. Am. J. Obstet. Gyn., 121:531-538.

Morris, W., ed. 1976. The American Heritage Dictionary of the English Language. Houghton Mifflin Company, Boston, Massachusetts. 1550 pp.

Muller, H. J., and E. Altenburg. 1919. The Rate of Change of Hereditary Factors in Drosophila. Proc. Soc. Exp. Biol. Med., 17:10-14.

Mumford, W. W. 1961. Some Technical Aspects of Microwave Radiation Hazards. Proc. IRE, 49:427-447.

Mumford, W. W. 1969. Heat Stress Due to RF Radiation. Proc. IEEE, 57:171-178.

Muraca, G. J., E. S. Ferri, and F. L. Buchta. 1976. A Study of the Effects of Microwave Irradiation of the Rat Testes. In: Biological Effects of Electromagnetic Waves, Vol. I., C. C. Johnson and M. L. Shore, eds. DHEW Publication (FDA) 77-8010. pp. 484-494.

NCRP. 1981. Radiofrequency Electromagnetic Fields, Properties, Quantities and Units, Biophysical Interaction and Measurements. NCRP Report No. 67, March 1, 1981. National Council on Radiation Protection and Measurements Publications, Washington, D.C. 134 pp.

Nieset, R. T., R. Baus, Jr., R. D. McAfee, J. J. Friedman, A. S. Hyde, and J. D. Fleming, Jr. 1958. Review of the Work Conducted at Tulane University. In: Proc. Second Tri-Service Conference on Biological Effects of Microwave Energy. (NTIS AD 131 477). pp. 202-214.

Nelson, A. J. M., and J. A. G. Holt. 1978. Combined Microwave Therapy. Med. J. Aust., 2:88-90.

O'Connor, M. E. 1980. Mammalian Teratogenesis and Radio-Frequency Fields. Proc. IEEE., 68:56-60.

Odland, L. T. 1973. Radio-Frequency Energy: A Hazard to Workers? Ind. Med. Surg., 42:23-26.

Olcerst, R. B., S. Belman, M. Eisenbud, W. W. Mumford, and J. R. Rabinowitz. 1980. The Increased Passive Efflux of Sodium and Rubidium from Rabbit Erythrocytes by Microwave Radiation. Radiat. Res., 82:244-256.

Oldendorf, W. H. 1970. Measurement of Brain Uptake of Radiolabeled Substances Using a Tritiated Water Internal Standard. Brain Res., 24:372-376.

Oliva, S. A., and G. N. Catravas. 1977. A Multiple-Animal Array for Equal Power Density Microwave Irradiation. IEEE Trans. Microwave Theory Techniques, MTT-25(5):433-436.

Olsen, R. G., J. L. Lords, and C. H. Durney. 1977. Microwave-Induced Chronotropic Effects in the Isolated Rat Heart. Ann. Biomed. Eng., 5:395-409.

Oscar, K. J., and T. D. Hawkins. 1977. Microwave Alteration of the Blood-Brain Barrier System of Rats. Brain Res., 126:281-293.

Oscar, K. J., S. P. Gruenau, M. T. Folker, and S. I. Rapoport. 1981. Local Cerebral Blood Flow after Microwave Exposure. Brain Res., 204:220-225.

Paff, G. H., R. J. Boucek, R. E. Nieman, and W. B. Deichmann. 1963. The Embryonic Heart Subjected to Radar. Anat. Rec., 147:379-385.

Parker, L. N. 1973. Thyroid Suppression and Adrenomedullary Activation by Low-Intensity Microwave Radiation. Am. J. Physiol., 224:1388-1390.

Paulsson, L-E., Y. Hamnerius, and W. G. McLean. 1977. The Effects of Microwave Radiation on Microtubules and Axonal Transport. Radiat. Res., 70:212-223.

Pavlov, I. P. 1960. Conditioned Reflexes (Translated by G. V. Anrep). Dover Publications, New York, New York. 430 pp.

Pay, T. L., E. C. Beyer, and C. F. Reichelderfer. 1972. Microwave Effects on Reproductive Capacity and Genetic Transmission in *Drosophila melanogaster*. J. Microwave Power, 7:75-82.

Pay, T. L., F. A. Andersen, and G. L. Jessup, Jr. 1978. A Comparative Study of the Effects of Microwave Radiation and Conventional Heating on the Reproductive Capacity of *Drosophila melanogaster*. Radiat. Res., 76:271-282.

Pazderova, J., R. Fisher, J. Formanek, J. John, E. Lucas, and V. Stýblová. 1969. Health State of Workers Exposed to Long-Term Electromagnetic Radiation of Order of Meter Waves. (In Czech.) Pracov. Lek., 21:346-361.

Pazderova-Vejlupkova, J., and M. Josifko. 1979. Changes in the Blood Count of Growing Rats Irradiated with a Microwave Pulse Field. Arch. Environ. Health, 34:44-50.

Pellon, J. R., K. M. Ulmer, and R. F. Gomez. 1980. Heat Damage to the Folded Chromosome of *Escherichia coli* K-12. Appl. Environ. Microbiol., 40(2): 358-364.

Pennes, H. H. 1948. Analysis of Tissue and Arterial Blood Temperatures in the Resting Human Forearm. J. Appl. Physiol., 1:93-122.

Perraud, J. 1976. Levels of Spontaneous Malformations in the CD Rat and CD-1 Mouse. Lab. Anim. Sci., 26(2):293-300.

Peterson, D. J., L. M. Partlow, and O. P. Gandhi. 1979. An Investigation of the Thermal and Athermal Effects of Microwave Irradiation on Erythrocytes. IEEE Trans. Biomed. Eng., BME-26:428-436.

Peto, R., M. C. Pike, P. Armitage, N. E. Breslow, D. R. Cox, S. V. Howard, N. Mantel, K. McPherson, J. Peto, and P. G. Smith. 1976. Design and Analysis of Randomised Clinical Trials Requiring Prolonged Observation of Each Patient. I. Introduction and Design. Br. J. Cancer, 34:585-612.

Peto, R., M. C. Pike, P. Armitage, N. E. Breslow, D. R. Cox, S. V. Howard, N. Mantel, K. McPherson, J. Peto, and P. G. Smith. 1977. Design and Analysis of Randomized Clinical Trials Requiring Prolonged Observation of Each Patient. II. Analysis and Examples. Br. J. Cancer, 35:1-39.

Phillips, R. D., E. L. Hunt, and N. W. King. 1975a. Field Measurements, Absorbed Dose, and Biologic Dosimetry of Microwaves. Ann. N.Y. Acad. Sci., 247:499-509.

Phillips, R. D., E. L. Hunt, R. D. Castro, and N. W. King. 1975b. Thermoregulatory, Metabolic, and Cardiovascular Response of Rats to Microwaves. J. Appl. Physiol., 38:630-635.

Pickard, W. F., and Y. H. Barsoum. 1981. Radio-Frequency Bioeffects at the Membrane Level: Separation of Thermal and Athermal Contributions in the Characeae. J. Membrane Biol., 61:39-54.

Pickard, W. F., and F. J. Rosenbaum. 1978. Biological Effects of Microwaves at the Membrane Level: Two Possible Athermal Electrophysiological Mechanisms and a Proposed Experimental Test. Math. Biosci., 39:235-253.

Pickard, W. F., Y. H. Barsoum, and F. J. Rosenbaum. 1980. Is the Characean Plasmalemma a Radio-Frequency Rectifier? (Abstract). Bioelectromagnetics, 1:216.

Pollak, M. 1965. On the Dielectric Dispersion of Polyelectrolytes with Application to DNA. J. Chem. Phys., 43:908-909.

Pollock, H. 1979. Epidemiologic Data on American Personnel in the Moscow Embassy. Bull. N.Y. Acad. Med., 55:1182-1186.

Prausnitz, S., and C. Süsskind. 1962. Effects of Chronic Microwave Irradiation on Mice. IRE Trans. on Biomedical Electronics, 9:104-108.

Preskorn, S. H., W. D. Edwards, and D. R. Justesen. 1978. Retarded Tumor Growth and Greater Longevity in Mice after Fetal Irradiation by 2450-MHz Microwaves. J. Surgical Oncology, 10:483-492.

Presman, A. S., and N. A. Levitina. 1962. Nonthermal Action of Microwaves on Cardiac Rhythm. Communication I. A Study of the Action of Continuous Microwaves. Bull. Exp. Biol. Med., 53:36-39.

Preston, E., and G. Prefontaine. 1980. Cerebrovascular Permeability to Sucrose in the Rat Exposed to 2,450-MHz Microwaves. J. Appl. Physiol., 49:218-223.

Preston, E., E. J. Vavasour, and H. M. Assenheim. 1979. Permeability of the Blood-Brain Barrier to Mannitol in the Rat Following 2450 MHz Microwave Irradiation. Brain Res., 174:109-117.

Prince, J. E., L. H. Mori, J. W. Frazer, and J. C. Mitchell. 1972. Cytologic Aspect of RF Radiation in the Monkey. Aerospace Med., 43:759-761.

Prohofsky, E. W., K. C. Lu, L. L. Van Zandt, and B. F. Putnam. 1979. Breathing Modes and Induced Resonant Melting of the Double Helix. Phys. Lett., 70A:492-494.

Pucak, G. J., C. S. Lee, and A. S. Zaino. 1977. Effects of Prolonged High Temperature on Testicular Development and Fertility in the Male Rat. Lab. Anim. Sci., 27(1):76-77.

Puska, P., J. Tuomilehto, J. Salonen, A. Nissinen, J. Virtamo, S. Björkqvist, K. Koskela, L. Neittaanmäki, T. Takalo, T. Kottke, J. Mäki, P. Sipilä, and P. Varvikko. 1978. The North Karelia Project: Evaluation of a Comprehensive Community Programme for Control of Cardiovascular Diseases in 1972-1977 in North Karelia, Finland. Research Institute for Community Health, University of Kuopio, Kuopio, Finland. 449 pp.

Rabinowitz, J. R. 1973. Possible Mechanisms for the Biomolecular Absorption on Microwave Radiation with Functional Implications. IEEE Trans. Microwave Theory and Techniques, MTT-21:850-851.

Reno, V. R. 1974. Microwave Reflection, Diffraction, and Transmission Studies of Man. Report NAMRL-1199. Naval Aerospace Medical Research Laboratory, Pensacola, Florida. 39 pp.

Richardson, A. W., T. D. Duane, and H. M. Hines. 1948. Experimental Lenticular Opacities Produced by Microwave Irradiations. Arch. Phys. Med., 29:765-769.

Rissman, W. J., and C. A. Cain. 1975. Microwave Hearing in Mammals. Proc. Nat. Elec. Cong., 30:239-244.

Roberti, B., G. H. Heebels, J. C. M. Hendricx, A. H. A. M. de Greef, and O. L. Wolthuis. 1975. Preliminary Investigations of the Effects of Low-Level Microwave Radiation and Spontaneous Motor Activity in Rats. Ann. N.Y. Acad. Sci., 247:417-424.

Roberts, N. J., Jr., and R. T. Steigbigel. 1977. Hyperthermia and Human Leukocyte Functions: Effects on Response of Lymphocytes to Mitogen and Antigen and Bactericidal Capacity of Monocytes and Neutrophils. Infect. Immun., 18:673-679.

Robinette, C. D., and C. Silverman. 1977. Causes of Death Following Occupational Exposure to Microwave Radiation (Radar) 1950-1974. In: Symposium on Biological Effects and Measurements of Radiofrequency/Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026, Rockville, Maryland. pp. 338-344.

Robinette, C. D., C. Silverman, and S. Jablon. 1980. Effects upon Health of Occupational Exposure to Microwave Radiation (Radar). Am. J. Epidemiol., 112:39-53.

Rosenthal, S. W., L. Birenbaum, I. T. Kaplan, W. Metlay, W. Z. Snyder, and M. M. Zaret. 1976. Effects of 35 and 107 GHz CW Microwaves on the Rabbit Eye. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010. pp. 110-128.

Roszkowski, W., J. K. Wrembel, K. Roszkowski, M. Janiak, and S. Szmigielski. 1980. The Search for an Influence of Whole-Body Microwave Hyperthermia on Anti-Tumor Immunity. J. Cancer Res. Clin. Oncol., 96:311-317.

Rotkovska, D., and A. Vacek. 1972. Effect of High-Frequency Electromagnetic Field Upon Haemopoietic Stem Cells in Mice. Folia Biologica (Praha), 18:292-297.

Rotkovska, D., and A. Vacek. 1975. The Effect of Electromagnetic Radiation on the Hematopoietic Stem Cells of Mice. Ann. N.Y. Acad. Sci., 247:243-250.

Rotkovska, D., and A. Vacek. 1977. Modification of Repair of X-Irradiation Damage of Hemopoietic System of Mice by Microwaves. J. Microwave Power, 12:119-123.

Rotkovska, D., J. Doubek, R. Rotkovsky, M. Stavratjev, and A. Vacek. 1973. Non-Contact Determination of Temperature Changes in Mice During Microwave Irradiation. Physiologia Bohemoslovaca, 22:359-363.

Rozzell, T. C., C. C. Johnson, C. H. Durney, J. L. Lords, and R. G. Olsen. 1974. A Nonperturbing Temperature Sensor for Measurements in Electromagnetic Fields. J. Microwave Power, 9(3):241-249.

Ruch, T. C., and H. D. Patton. 1973. Medical Physiology and Biophysics, 20th ed. Saunders, Philadelphia, Pennsylvania.

Rudnev, M., A. Bokina, N. Eksler, and M. Navakatikyan. 1978. The Use of Evoked Potential and Behavioral Measures in the Assessment of Environmental Insult. In: Multidisciplinary Perspectives in Event-Related Brain Potential Research, D. A. Otto, ed. EPA-600/9-77-043, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina. pp. 444-447.

Rudge, A. W. 1970. An Electromagnetic Radiation Probe for Near-Field Measurements at Microwave Frequencies. J. Microwave Power, 5(3):155-174.

Ruggera, P. S. 1976. E- and H-Field Instrumentation and Calibration below 500 MHz. In: Biological Effects of Electromagnetic Waves. Vol. II, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8011, Rockville, Maryland. pp. 281-296.

Rugh, R. 1976a. Are Mouse Fetuses Which Survive Microwave Radiation Permanently Affected Thereby? Health Phys., 31:33-39.

Rugh, R. 1976b. The Relation of Sex, Age, and Weight of Mice to Microwave Radiation Sensitivity. J. Microwave Power, 11(2):127-132.

Rugh, R., and M. McManaway. 1976. Anesthesia as an Effective Agent Against the Production of Congenital Anomalies in Mouse Fetuses Exposed to Electromagnetic Radiation. J. Exp. Zool., 197:363-368.

Rugh, R., and M. McManaway. 1977. Mouse Fetal Sensitivity to Microwave Radiation. Cong. Anom., 17:39-45.

Rugh, R., E. I. Ginns, H. S. Ho, and W. M. Leach. 1974. Are Microwaves Teratogenic? In: Biologic Effects and Health Hazards of Microwave Radiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess, and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 98-107.

Rugh, R., E. I. Ginns, H. S. Ho, and W. M. Leach. 1975. Responses of the Mouse to Microwave Radiation During Estrous Cycle and Pregnancy. Radiat. Res., 62:225-241.

Rukspollmuang, S., and K. M. Chen. 1979. Heating of Spherical Versus Realistic Models of Human and Infrahuman Heads by Electromagnetic Waves. Radio Sci., 14(6S):51-62.

Ruppin, R. 1979. Electromagnetic Power Deposition in a Dielectric Cylinder in the Presence of a Reflecting Surface. IEEE Trans. Microwave Theory Techniques, MTT-27(11):910-914.

Sams & Co. 1975. Reference Data for Radio Engineers. Howard W. Sams & Co., Inc., New York, New York. Chapter 1.

Sams & Co. 1981. Reference Data for Radio Engineers. Howard W. Sams & Co., Inc., New York, New York. Chapter 1.

Sanders, A. P., D. J. Schaefer, and W. T. Joines. 1980. Microwave Effects on Energy Metabolism of Rat Brain. Bioelectromagnetics 1:171-181.

Sanza, J. N., and J. de Lorge. 1977. Fixed Interval Behavior of Rats Exposed to Microwaves at Low Power Densities. Radio Sci., 12(6S):273-277.

Scholl, D. M., and S. J. Allen. 1979. Skilled Visual-Motor Performance by Monkeys in a 1.2-GHz Microwave Field. Radio Sci., 14(6S):247-252.

Schrot, J., J. R. Thomas, and R. A. Banvard. 1980. Modification of the Repeated Acquisition of Response Sequences in Rats by Low-Level Microwave Exposure. Bioelectromagnetics, 1:89-99.

Schwan, H. P. 1957. Electrical Properties of Tissue and Cell Suspensions. Adv. Biol. Med. Phys., 5:147-209.

Schwan, H. P. 1965. Electrical Properties of Bound Water. Ann. N.Y. Acad. Sci., 125:344-354.

Schwan, H. P., and K. R. Foster. 1980. RF-Field Interactions with Biological Systems: Electrical Properties and Biophysical Mechanisms. Proc. IEEE, 68:104-113.

Schwan, H. P., and K. Li. 1956. The Mechanism of Absorption of Ultrahigh Frequency Electromagnetic Energy in Tissues as Related to the Problem of Tolerance Dosage. IRE Trans. Med. Electron., 4:45-49.

Schwan, H. P., A. Anne, and L. Sher. 1966. Heating of Living Tissues. Report NAEC-ACEL-534, U.S. Naval Air Engineering Center, Philadelphia, Pennsylvania. 30 pp.

Schwarz, G. 1967. On Dielectric Relaxation Due to Chemical Rate Processes. J. Phys. Chem., 71:4021-4030.

Schwarz, G. 1972. Dielectric Relaxation of Biopolymers in Solution. Adv. Mol. Relaxation Processes, 3:281-295.

Schwarz, G., and J. Seelig. 1968. Kinetic Properties and the Electric Field Effect of the Helix-Coil Transition of Poly (γ-Benzyl L-Glutamate) Determined from Dielectric Realization Measurements. Biopolymers, 6:1263-1277.

Seaman, R. L., and H. Wachtel. 1978. Slow and Rapid Responses to CW and Pulsed Microwave Radiation by Individual Aplysia Pacemakers. J. Microwave Power, 13:77-86.

Servantie, B., G. Bertharion, R. Joly, A. Servantie, J. Etienne, P. Dreyfus, and P. Escoubet. 1974. Pharmacologic Effects of a Pulsed Microwave Field. In: Biologic Effects and Health Hazards of Microwave Radiation, P. Czerski, K. Ostrowski, M. L. Shore, C. Silverman, M. J. Suess, and B. Waldeskog, eds. Polish Medical Publishers, Warsaw, Poland. pp. 36-45.

Shacklett, D. E., T. J. Tredici, and D. L. Epstein. 1975. Evaluation of Possible Microwave-Induced Lens Changes in the United States Air Force. Aviat. Space Environ. Med., 46:1403-1406.

Shah, S. A., and J. A. Dickson, 1978a. Effect of Hyperthermia on the Immune Response of Normal Rabbits. Cancer Res., 38:3518-3522.

Shah, S. A., and J. A. Dickson. 1978b. Effect of Hyperthermia on the Immunocompetence of VX2 Tumor-Bearing Rabbits. Cancer Res., 38:3523-3531.

Shandala, M. G., M. I. Rudnev, and M. A. Navakatian. 1977. Patterns of Change in Behavioral Reactions to Low Power Densities of Microwaves (Abstract). International Symposium on the Biological Effects of Electromagnetic Waves (URSI), Airlie, Virginia. p. 88.

Shelton, W. W., Jr., and J. H. Merritt. 1981. In Vitro Study of Microwave Effects on Calcium Efflux in Rat Brain Tissue. Bioelectromagnetics, 2:161-167.

Sheppard, A. R., S. M. Bawin, and W. R. Adey. 1979. Models of Long-Range Order in Cerebral Macromolecules: Effect of Sub-ELF and of Modulated VHF and UHF Fields. Radio Sci., 14(6S):141-145.

Sher, L. D. 1970. Interaction of Microwave and RF Energy on Biological Material. In: Electronic Product Radiation and the Health Physicist. Report BRH/DEP 70-26, HEW, Bureau of Radiological Health, Rockville, Maryland. pp. 431-462.

Sheridan, J. P., B. P. Gaber, F. Cavatorta, and P. E. Schoen. 1979. Molecular Level Effects of Microwaves on Natural and Model Membranes: A Raman Spectroscopic Investigation (Abstract). Joint Meeting of USNC/URSI and the Bioelectromagnetics Society, Seattle, Washington. p. 468.

Sherins, R. J., D. Brightwell, and P. M. Sternthal. 1977. Longitudinal Analysis of Semen in Fertile and Infertile Men. In: The Testes in Normal and Infertile Men, P. Troen and H. R. Nankin, eds. Raven Press, New York, New York. pp. 473-488.

Shore, M. L., R. P. Felten, and A. Lamanna. 1977. The Effect of Repetitive Prenatal Low-Level Microwave Exposure on Development in the Rat. In: Symposium on Biological Effects and Measurement of Radio Frequency/ Microwaves, D. G. Hazzard, ed. HEW Publication (FDA) 77-8026, Rockville, Maryland. pp. 280-289.

Siekierzynski, M., P. Czerski, H. Milczsret, A. Gidynski, C. Czarnecki, E. Dziuk, and W. Jedrzejczak. 1974a. Health Surveillance of Personnel Occupationally Exposed to Microwaves. II. Functional Disturbances. Aerospace Med., 45:1143-1145.

Siekierzynski, M., P. Czerski, A. Gidynski, S. Zydecki, C. Czarnecki, E. Dziuk, and W. Jedrezejczak. 1974b. Health Surveillance of Personnel Occupationally Exposed to Microwaves. III. Lens Translucency. Aerospace Med., 45:116-1148.

Siems, L. L., A. J. Kosman, and S. L. Osborne. 1948. A Comparative Study of Short Wave and Microwave Diathermy on Blood Flow. Arch. Phys. Med., 29:759-764.

Sigler, A. T., A. M. Lilienfeld, B. H. Cohen, and J. E. Westlake. 1965. Radiation Exposure in Parents of Children with Mongolism (Down's Syndrome). Bull. J. Hopkins Hosp., 117:374-399.

Silverman, C. 1979. Epidemiologic Approach to the Study of Microwave Effects. Bull. N.Y. Acad. Med., 55:1166-1181.

Silverman, C. 1980. Epidemiologic Studies of Microwave Effects. Proc. IEEE, 68:78-84.

Smialowicz, R. J. 1976. The Effect of Microwaves (2450 MHz) on Lymphocyte Blast Transformation In Vitro. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 472-483.

Smialowicz, R. J., J. B. Kinn, and J. A. Elder. 1979a. Perinatal Exposure of Rats to 2450-MHz CW Microwave Radiation: Effects on Lymphocytes. Radio Sci., 14(6S):147-153.

Smialowicz, R. J., M. M. Riddle, P. L. Brugnolotti, J. M. Sperrazza, and J. B. Kinn. 1979b. Evaluation of Lymphocyte Function in Mice Exposed to 2450 MHz (CW) Microwaves. In: Electromagnetic Fields in Biological Systems, S. S. Stuchly, ed. The International Microwave Power Institute, Edmonton, Canada. pp. 122-152.

Smialowicz, R. J., J. S. Ali, E. Berman, S. J. Bursian, J. B. Kinn, C. G. Liddle, L. W. Reiter, and C. M. Weil. 1981a. Chronic Exposure of Rats to 100-MHz (CW) Radiofrequency Radiation: Assessment of Biological Effects. Radiat. Res., 86:488-505.

Smialowicz, R. J., M. M. Riddle, P. L. Brugnolotti, R. R. Rogers, and K. L. Compton. 1981b. Detection of Microwave Heating in 5-Hydroxytryptamine-Induced Hypothermic Mice. Radiat. Res., 88:108-117.

Smialowicz, R. J., C. M. Weil, J. B. Kinn, and J. A. Elder. 1982. Exposure of Rats to 425-MHz (CW) Radiofrequency Radiation: Effects on Lymphocytes. J. Microwave Power, 17:211-221.

Smith, J. B., R. P. Knowlton, and S. S. Agarwal. 1978. Human Lymphocyte Responses are Enhanced by Culture at 40 °C. J. Immunol., 121:691-694.

Smith, P. E., and E. W. James. 1964. Human Responses to Heat Stress. Arch. Environ. Health, 9:332-342.

Smolyanskaya, A. Z., and R. L. Vilenskaya. 1973. Effects of Millimeter-Band Electromagnetic Radiation on the Functional Activity of Certain Genetic Elements of Bacterial Cells. Usp Fiz. Nauk, 110:571-572. (Trans. in Soviet Physics Uspekhi, 16(4):571-572, 1974.)

Snyder, S. H. 1971. The Effect of Microwave Irradiation on the Turnover Rate of Serotonin and Norepinephrine and the Effect of Monoamine Metabolizing Enzymes. Final Report, Contract No. DADA 17-69-C-9144, U.S. Army Medical Research and Development Command, Washington, D.C. (NTIS AD-729 161). 26 pp.

Sommer, H. C., and H. E. von Gierke. 1964. Hearing Sensations in Electric Fields. Aerospace Med., 35:834-839.

Spalding, J. F., R. W. Freyman, and L. M. Holland. 1971. Effects of 800-MHz Electromagnetic Radiation on Body Weight, Activity, Hematopoiesis and Life Span in Mice. Health Phys., 20:421-424.

Spiegel, R. J., D. M. Deffenbaugh, and J. E. Mann. 1979. Modeling Heat Transfer in Man Exposed to an Electromagnetic Field. Final Tech. Report No. 14-9239, Southwest Research Institute, San Antonio, Texas. 106 pp.

Spiegel, R. J., D. M. Deffenbaugh, and J. E. Mann. 1980a. A Thermal Model of the Human Body Exposed to an Electromagnetic Field. Bioelectromagnetics, 1(3):253-270.

Spiegel, R. J., W. E. Oakey, and E. L. Bronaugh. 1980b. A Variable-Volume Cavity Electromagnetic Near-Field Simulator. IEEE Trans. Electromagnetic Compatibility, EMC-22(4):289-297.

Stavinoha, W. B., A. Modak, M. A. Medina, and A. E. Gass. 1975. Growth and Development of Neonatal Mice Exposed to High-Frequency Electromagnetic Fields. NTIS Document No. AD-A022 765. 12 pp.

Stern, S., L. Margolin, B. Weiss, S. Lu, and S. M. Michaelson. 1979. Microwaves: Effect on Thermoregulatory Behavior in Rats. Science, 206:1198-1201.

Stodolnik-Baranska, W. 1967. Lymphoblastoid Transformation of Lymphocytes In Vitro after Microwave Irradiation. Nature, 214:102-103.

Stolwijk, J. A. J. 1969. Expansion of a Mathematical Model of Thermoregulation to Include High Metabolic Rates. NASA CR-102192 (NTIS N70-19831), Washington, D.C. 120 pp.

Stolwijk, J. A. J. 1971. A Mathematical Model of Physiological Temperature Regulation in Man. NASA CR-1855 (NTIS N71-33401), Washington, D.C. 76 pp.

Stolwijk, J. A. J., and D. J. Cunningham. 1968. Expansion of a Mathematical Model of Thermoregulation to Include High Metabolic Rates. NASA CR-92443 (NTIS N69-16568), Washington, DC. 133 pp.

Stolwijk, J. A. J., and J. D. Hardy. 1966. Temperature Regulation in Man - A Theoretical Study. Pflugers Arch., 291:129-162.

Stolwijk, J. A. J., and J. D. Hardy. 1977. Control of Body Temperature. In: Handbook of Physiology - Reactions to Environmental Agents, Douglas H. K. Lee, ed. Williams and Wilkins, Baltimore, Maryland. Ch. 4, pp. 45-68.

Stratton, J. A. 1941. Electromagnetic Theory. McGraw-Hill, New York, New York. pp. 414-420.

Stuchly, M. A., and S. S. Stuchly. 1980. Dielectric Properties of Biological Substances - Tabulated. J. Microwave Power, 15(1):19-26.

Sulek, K., C. J. Schlagel, W. Wiktor-Jedrzecjzak, H. S. Ho, W. M. Leach, A. Ahmed, and J. N. Woody. 1980. Biologic Effects of Microwave Exposure. I. Threshold Conditions for the Induction of the Increase in Complement Receptor Positive (CR^+) Mouse Spleen Cells Following Exposure to 2450-MHz Microwaves. Radiat. Res., 83:127-137.

Susskind, C. 1962. Nonthermal Effects of Microwave Radiation. Report RADC-TDR-62-624, Annual Scientific Report (1961-62) on Contract No. NONR-222(92) and Final Report on Contract AF41(657)-114, University of California, Electronics Research Laboratory, Berkeley, California. 25 pp.

Susskind, C. 1975. Correspondence on D. R. Justesen's "Prescriptive Grammar for the Radiobiology of Nonionizing Radiation." J. Microwave Power, 10(4):357.

Sutton, C. H., and F. B. Carroll. 1979. Effects of Microwave-Induced Hyperthermia on the Blood-Brain Barrier of the Rat. Radio Sci., 14:329-334.

Swicord, M. L. 1971. Microwave Measurements and New Types of Detectors for Evaluation of Health Hazards. BRH/DEP Publication No. 71-1. U.S. Department of Health, Education and Welfare, Public Health Service, Rockville, Maryland. 33 pp.

Switzer, W. G., and D. S. Mitchell. 1977. Long-Term Effects of 2.45-GHz Radiation on the Ultrastructure of the Cerebral Cortex and on Hematologic Profiles of Rats. Radio Sci., 12:287-293.

Szmigielski, S. 1975. Effect of 10-cm (3 GHz) Electromagnetic Radiation (Microwaves) on Granulocytes In Vitro. Ann. N.Y. Acad. Sci., 247:275-281.

Szmigielski, S., J. Jeljaszewicz, and M. Wiranowska. 1975. Acute Staphylococcal Infections in Rabbits Irradiated with 3-GHz Microwaves. Ann. N.Y. Acad. Sci., 247:305-311.

Szmigielski, S., M. Kobus, and M. Janiak. 1976. Enhanced Cytotoxic Effect of Hyperthermia (43°C) on Colcemide-Treated Normal and SV_{40}-Transformed Cells Grown In Vitro. Z. Geschwulstkrankh., 47:396-399.

Szmigielski, S., G. Pulverer, W. Hryniewicz, and M. Janiak. 1977. Inhibition of Tumor Growth in Mice by Microwave Hyperthermia, Streptolysin S and Colcemide. Radio Sci., 12(6S):185-189.

Szmigielski, S., M. Janiak, W. Hryniewicz, J. Jeljaszewicz, and G. Pulverer. 1978. Local Microwave Hyperthermia (43°C) and Stimulation of the Macrophage and T-Lymphocyte Systems in Treatment of Guérin Epithelioma in Rats. Z. Krebsforsch., 91:35-48.

Szmigielski, S., A. Szydzinski, A. Pietraszek, and M. Bielec. 1980. Acceleration of Cancer Development in Mice by Long-Term Exposition to 2450-MHz Microwave Fields. In: URSI International Symposium Proceedings, Ondes Electromagnetiques et Biologie, A. J. Berteaud and B. Servantie, eds. Paris, France. pp. 165-169.

Takashima, S. 1963. Dielectric Dispersion of DNA. J. Mol. Biol., 7:455-467.

Takashima, S., and A. Minikata. 1975. Dielectric Behavior of Biological Macromolecules. Digest of Literature on Dielectrics, 37:602-653 (NAS, Washington, D.C.).

Takashima, S., B. Onaral, and H. P. Schwan. 1979. Effects of Modulated RF Energy on the EEG of Mammalian Brains. Radiat. Environ. Biophys., 16:15-27.

Taylor, C. R., K. Schmidt-Nielsen, and J. L. Raab. 1970. Scaling of Energetic Cost of Running to Body Size in Mammals. Am. J. Physiol., 219:1104-1107.

Taylor, E. M., and B. T. Ashleman. 1974. Analysis of Central Nervous System Involvement in the Microwave Auditory Effect. Brain Res., 74:201-208.

Tell, R. 1972. Microwave Energy Absorption in Tissue. EPA Report PB 208-233, U.S. Environmental Protection Agency, Washington, D.C. 53 pp.

Tell, R. A., and F. Harlen. 1979. A Review of Selected Biological Effects and Dosimetric Data Useful for Development of Radiofrequency Safety Standards for Human Exposure. J. Microwave Power, 14:405-424.

Thomas, J. R., and G. Maitland. 1979. Microwave Radiation and Dextroamphetamine: Evidence of Combined Effects on Behavior of Rats. Radio Sci., 14:253-258.

Thomas, J. R., E. D. Finch, D. W. Fulk, and L. S. Burch. 1975. Effects of Low-Level Microwave Radiation on Behavioral Baselines. Ann. N.Y. Acad. Sci., 247:425-432.

Thomas, J. R., S. S. Yeandle, and L. S. Burch. 1976. Modification of Internal Discriminative Stimulus Control of Behavior by Low Levels of Pulsed Microwave Radiation. In: Biological Effects of Electromagnetic Waves, Vol. I., C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 201-214.

Thomas, J. R., L. S. Burch, and S. S. Yeandle. 1979. Microwave Radiation and Chlordiazepoxide: Synergistic Effects on Fixed-Interval Behavior. Science, 203:1357-1358.

Thomas, J. R., J. Schrot, and R. A. Banvard. 1980. Behavioral Effects of Chlorpromazine and Diazepam Combined with Low-Level Microwaves. Neurobehav. Toxicol., 2:131-135.

Thomson, R. A. E., S. M. Michaelson, and J. W. Howland. 1965. Modification of X-Irradiation Lethality in Mice by Microwaves (Radar). Radiat. Res., 24: 631-635.

Tinney, C. E., J. L. Lords, and C. H. Durney. 1976. Rate Effects in Isolated Turtle Hearts Induced by Microwave Irradiation. IEEE Trans. Microwave Theory Techniques, MTT-24:18-24.

Tolgskaya, M. S., and Z. V. Gordon. 1973. Pathological Effects of Radio Waves. (Trans. from Russian by B. Haigh.) LC Cat. Card 72-94825. Consultants Bureau, New York, New York. pp. 63-106.

Tyazhelov, V. V., S. I. Alekseyev, and P. A. Grigor'ev. 1979a. Change in the Conductivity of Phospholipid Membranes Modified by Alamethicin on Exposure to a High Frequency Electromagnetic Field. Biophysics, 23:750-751. (Trans. of Biofizika, 23:732-733, 1978.)

Tyazhelov, V. V., R. E. Tigranian, E. O. Khizhniak, and I. G. Akoev. 1979b. Some Peculiarities of Auditory Sensations Evoked by Pulsed Microwave Fields. Radio Sci., 14(6S):259-263.

United States Senate Committee on Commerce, Science, and Transportation. 1979. Microwave Irradiation of the U.S. Embassy in Moscow. U.S. Government Printing Office, Washington, D.C. 26 pp.

VanDemark, N. L., and M. J. Free. 1970. Temperature Effects. In: The Testis, Vol. III, A. D. Johnson, W. R. Gomes, and N. L. VanDemark, eds. Academic Press, New York, New York. Chapter 7, pp. 233-312.

Varma, M. M., and E. A. Traboulay, Jr. 1975. Biological Effects of Microwave Radiation on the Testes of Swiss Mice. Experientia, 31:301-302.

Varma, M. M., and E. A. Traboulay, Jr. 1976. Evaluation of Dominant Lethal Test and DNA Studies in Measuring Mutagenicity Caused by Non-Ionizing Radiation. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 386-396.

Varma, M. M., and E. A. Traboulay. 1977. Comparison of Native and Microwave Irradiated DNA. Experientia, 33:1649-1650.

Varma, M. M., E. L. Dage, and S. R. Joshi. 1976. Mutagenicity Induced by Non-Ionizing Radiation in Swiss Male Mice. In: Biological Effects of Electromagnetic Waves, Vol. I, C. C. Johnson and M. L. Shore, eds. HEW Publication (FDA) 77-8010, Rockville, Maryland. pp. 397-405.

Vendrik, A. J. H., and J. J. Vos. 1958. Comparison of the Stimulation of the Warmth Sense Organ by Microwave and Infrared. J. Appl. Physiol., 13:435-444.

Wachtel, H., R. Seaman, and W. Joines. 1975. Effects of Low-Intensity Microwaves on Isolated Neurons. Ann. N.Y. Acad. Sci., 247:46-62.

Wakim, K. G., J. W. Gersten, J. F. Herrick, E. C. Elins, and F. H. Krusen. 1948. The Effects of Diathermy on the Flow of Blood in the Extremities. Arch. Phys. Med., 29:583-593.

Wangemann, R. T., and S. F. Cleary. 1976. The In Vivo Effects of 2.45 GHz Microwave Radiation on Rabbit Serum Components and Sleeping Times. Radiat. Environ. Biophys., 13:89-103.

Ward, T. R., J. W. Allis, and J. A. Elder. 1975. Measure of Enzymatic Activity Coincident with 2450 MHz Microwave Exposure. J. Microwave Power, 10:315-320.

Weil, C. M. 1974. Propagation of Plane Waves Through Two Parallel Dielectric Sheets. IEEE Trans. Biomed. Eng., BME-21(2):165-168. (Addendum and Corrections, BME-24(1):78-80, 1977.)

Weil, C. M. 1975. Absorption Characteristics of Multilayered Sphere Models Exposed to UHF/Microwave Radiation. IEEE Trans. Biomed. Eng., BME-22(6):468-476.

Weil, C. M. 1977. Review of Exposure Techniques and Dosimetric Methods Employed in Microwave Bioeffects Research. Proceedings of IEEE Region III Conference (Southeastern), Williamsburg, Virginia. Cat. No. 77 CHO 1233-6 Region III. pp. 507-510.

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W. M. Leach, and K. W. Sell. 1977a. Immune Response of Mice at 2450-MHz Microwave Radiation:

Overview of Immunology and Empirical Studies of Lymphoid Splenic Cells. Radio Sci., 12(6S):209-219.

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W. M. Leach, and K. W. Sell. 1977b. Increase in the Frequency of Fc Receptor (FcR) Bearing Cells in the Mouse Spleen Following a Single Exposure of Mice to 2450 MHz Microwaves. Biomedicine, 27:250-252.

Wiktor-Jedrzejczak, W., A. Ahmed, K. W. Sell, P. Czerski, and W. M. Leach. 1977c. Microwaves Induce an Increase in the Frequency of Complement Receptor-Bearing Lymphoid Spleen Cells in Mice. J. Immunol., 118:1499-1502.

Williams, D. B., J. P. Monalen, W. J. Nicholson, and J. J. Aldrich. 1955. Biologic Effects Studies on Microwave Radiation. AMA Arch. Ophth., 54:863-874.

Wilson, B. S., J. M. Zook, W. T. Joines, and J. H. Casseday. 1980. Alterations in Activity at Auditory Nuclei of the Rat Induced by Exposure to Microwave Radiation: Autoradiographic Evidence Using [^{14}C]2-Deoxy-D-Glucose. Brain Res., 187:291-306.

Wilson, J. G. 1973. Environment and Birth Defects. Academic Press, New York, New York. 305 pp.

Wissler, E. H. 1961. Steady-State Temperature Distribution in Man. J. Appl. Physiol., 16:734-740.

Wissler, E. H. 1964. A Mathematical Model of the Human Thermal System. Bull. Math. Biophys., 26:147-166.

Wyndham, C. H., and A. R. Atkins. 1960. An Approach to the Solution of the Human Biothermal Problem with the Aid of an Analog Computer. Proc. 3rd Int. Conf. Medical Electronics, London, England.

Yamaura, I., and S. Chichibu. 1967. Super-High Frequency Electric Field and Crustacean Ganglionic Discharges. Tohoku J. Exp. Med., 93:249-259.

Youmans, H. D., and H. S. Ho. 1975. Development of Dosimetry for RF and Microwave Radiation-I: Dosimetric Quantities for RF and Microwave Electromagnetic Fields. Health Phys., 29:313-316.

Zamenhof, S., and S. Greer. 1958. Heat as an Agent Producing High Frequency of Mutations and Unstable Genes in Escherichia coli. Nature, 182(4635): 611-613.

Zaret, M. M. 1976. Electronic Smog as a Potentiating Factor in Cardiovascular Disease: A Hypothesis of Microwaves as an Etiology for Sudden Death from Heart Attack in North Karelia. Med. Res. Eng., 12:13-16.

Zeman, G. H., R. L. Chaput, Z. R. Glazer, and L. C. Gershman. 1973. Gamma-Aminobutyric Acid Metabolism in Rats Following Microwave Exposure. J. Microwave Power, 8:213-216.

GLOSSARY

ABSORPTION   The irreversible conversion of electromagnetic energy into other forms of energy as a result of interaction with matter. See SPECIFIC ABSORPTION and SPECIFIC ABSORPTION RATE.

α-HELIX   A conformation found in protein molecules where the amino acid chain turns in a helical pattern with weak chemical bonds (hydrogen bonds) forming between successive turns in the helix.

AMES TEST   A standard test for mutagenic potential of various agents performed with specialized strains of bacteria.

ANECHOIC CHAMBER   A chamber lined with material that absorbs RF radiation; an RF-exposure system free of scattered and reflected radiation.

ANGULAR MOMENTUM   The quantity of motion of a rotating body - directly proportional to the angular velocity of the rotating body.

ANTENNA   A device for radiating or receiving radio waves.

ANTENNA REGIONS   The distinction between electromagnetic fields far from and those near to the antenna. The regions are usually classified into three zones: near (static) zone, intermediate (induction) zone, and far (radiation) zone. The zones are spatially located by drawing spheres of different radii around the antenna. The radii are approximately $r < \lambda$ for the near zone, $\lambda < r(\lambda)$ for the intermediate zone, and $r > \lambda$ for the far zone. Note that λ is the wavelength of the electromagnetic field produced by the antenna. In the far zone the field components (E and H) lie transverse to the direction of the propagation, and the shape of the field pattern is independent of the radius at which it is taken. In the near and intermediate zones the field patterns are quite complicated, and the shape is, in general, a function of the radius and angular position (azimuth and elevation) in front of the antenna.

ATHERMAL EFFECT (NONTHERMAL EFFECT)   Any effect of electromagnetic energy on a body that is not a heat-related effect.

ATTENUATION   A general term used to denote a decrease in magnitude of RF transmission from one point to another.

AUTOLYSIS   The decomposition of an organ or tissue by its own enzymes.

AVERAGE POWER $\bar{W}$ The time-average rate of energy transfer:

$$\bar{W} = 1/(t_2 - t_1) \int_{t}^{t^2} W(t)dt$$

For radar calculations, average power $\bar{W}$ = peak power x pulse width x pulse repetition frequency.

BASES Biochemical compounds, either purine or pyrimidines, that are ring structures containing carbon and nitrogen and which are capable of weak bonding to each other.

β-SHEET A conformation found in protein molecules where two or more portions of amino acid chains line up side-to-side, with weak hydrogen bonds forming between adjacent chains.

BIOPOLYMER A polymeric substance formed in a biological system, e.g., DNA, proteins.

BLASTOGENIC RESPONSE The transformation of small lymphocytes into large morphologically primitive blast-like cells capable of undergoing mitosis; this phenomenon can be induced in cultured by a variety of agents, including mitogens as well as antigens, to which the cell donor has been previously immunized.

BLOOD-BRAIN BARRIER A functional concept to explain the observation that many substances transported by blood readily enter other tissues but do not enter the brain. The barrier functions as if it were a continuous membrane lining the brain vasculature.

BURSA OF FABRICUS A lymphoidal organ in the hindgut of birds that influences B cell development.

CALCIUM EFFLUX The release of calcium ions from a sample into a surrounding solution.

CALORIE The amount of heat necessary to raise the temperature of one gram of water 1 °C. One calorie equals 4.184 joules.

CARCINOMA Any of the various types of malignant neoplasm derived from epithelial tissue, occurring more frequently in the skin, bronchi, stomach, and prostate gland in men, and in the breast, cervix, and skin in women.

CATARACTOGENIC Giving rise to the formation of a cataract, an opacity in the crystalline lens of the eye.

CHEMOSIS Excessive edema of the ocular conjunctiva.

CHROMOSOMES Large complex biochemical structures, containing nucleic acid (DNA) and proteins, which can be visualized in some cells by certain light microscopy techniques.

CIRCULARLY POLARIZED If the electric field is viewed as a point in space, the locus of the end point of the vector will rotate and trace out an ellipse once each cycle.

COLONY-FORMING UNIT (CFU) Colonies of bone marrow or blood cells arising from a single progenitor cell when grown *in vitro* or *in vivo*.

COMPLEX DIELECTRIC PERMITTIVITY The characterization of electrical parameters of materials at the macroscopic level.

CONFORMATION The spatial distribution of the parts of a macromolecule in relation to each other, i.e., how a chain of amino acids folds on itself to form a protein.

CONTINUOUS WAVE (CW) Electromagnetic fields that vary sinusoidally in time; that is, those fields which oscillate at a single frequency.

COUNTER-CURRENT HEAT EXCHANGE The heat exchange between blood flowing in opposite directions at different temperatures, e.g., adjacent arteries and veins.

CORE TEMPERATURE The temperature near the center of the body; usually measured through the rectum.

CYTOSIS Increase in number of cells, e.g., leukocytosis, increase in the total number of circulating leukocytes.

DEBYE A unit for dipole moment equal to the dipole moment of a charge distribution of one positive and one negative charge, each equal in magnitude to the charge of an electron separated by 1 A (10^{-10} m).

DECIBEL (dB) A unit expressing the logarithmic ratio of two powers or voltages. One tenth of a Bel.

DENSITOMETRY The measurement of exposure to an RF field; usually expressed in units of milliwatts per square centimeter.

DEPTH OF PENETRATION For a plane wave electromagnetic field incident on the boundary of a good conductor, the depth of penetration of the wave is that depth at which the field strength of the wave has been reduced to 1/e or approximately 37% of its original value.

DIELECTRIC MATERIAL A class of materials that act as electric insulators. For this class the conductivity is presumed to be zero, or very small. The positive and negative charges in dielectrics are tightly bound together so that there is no actual transport of charge under the influence of a field. Such material alters electromagnetic fields because of induced charges formed by the interaction of the dielectric with the incident field.

DIPOLE A molecule (or other structure) having the effective centers of positive and negative charges separated.

DIPOLE MOMENT A quantity describing the strength of a particular dipole:

$$\vec{d} = \int_V \rho(\vec{r})\, \vec{r}\, d\vec{r}$$

where the dipole ($\vec{d}$) is the integral of the charge distribution ($\rho(\vec{r})$) times the vector distance ($\vec{r}$) from a designated origin over the entire space containing the charge distribution (v).

DNA Deoxyribonucleic acid; the chemical which makes up the genes, the basic unit of heredity.

DNA MELTING CURVE Characteristic loss of helical structure and separation of the strands of a DNA molecule when temperature is raised.

DOSIMETRY The measurement of the absorbed dose or dose rate by an object in a radiofrequency field; usually expressed as watts per kilogram or joules per kilogram.

DUTY FACTOR (CYCLE) The product of the pulse duration and the pulse repetition frequency.

ELECTRIC FIELD STRENGTH The force on a stationary unit positive charge at a point in an electric field. This force may be measured in volts per meter (V/m).

ELECTROMAGNETIC RADIATION (EMR) Energy in the form of electric and magnetic fields.

ELECTROMAGNETIC WAVE A wave characterized by variations of electric and magnetic fields. Electromagnetic waves are categorized as radio waves, light rays, etc., depending on the frequency.

ELECTROPHORETIC MOBILITY The ability of a cell or macromolecule to move in response to a constant electric field.

ELECTROSTRICTIVE FORCE Force exerted by an electrostatic field that causes the elastic deformation of a dielectric.

ELLIPSOID SHAPE A surface, all plane sections of which are ellipses or circles.

ENZYME KINETICS (ACTIVITY) Measure of how rapidly an enzyme catalyzes a chemical reaction.

EPITHELIOMA Carcinoma derived from squamous cells (scale-like cells) or from the basal and adnexal cells (accessory cells) of the skin.

ERYTHROPOIESIS The production of red blood cells.

EUKARYOTE An organism composed of one or more complex cells containing chromosomes that are segregated from the rest of the cell by a nuclear membrane. This distinction is in contrast to bacteria, which have less complex DNA structure distributed throughout the cell volume.

EXCITATION The absorption of energy by a molecule or other structure.

FAR FIELD REGION See antenna regions.

FIELD-INDUCED MIGRATION The physical movement of charged bodies under the influence of an electromagnetic field.

50TH PERCENTILE For a large set of measurements arranged in order of magnitude, the 50% percentile is the value such that 50% of the measurements are less than that value and 50% are greater.

FINITE DIFFERENCE TECHNIQUE The approximation of differentials by their finite difference; e.g., $dy/dx \sim \Delta y/\Delta x$.

FIRST-ORDER DIFFERENTIAL EQUATION A differential equation of order one (only single-order derivatives are included in the equation).

FREQUENCY The number of sinusoidal cycles made by electromagnetic radiation in one second; usually expressed in units of hertz.

GIGAHERTZ (GHz) One billion cycles per second.

HERTZ (Hz) One cycle per second.

HISTOPATHOLOGY The department of pathology concerned with minute structure, composition, and function of diseased tissues; microscopic pathology.

HUMORAL Relating to the extracellular fluids of the body, i.e., blood and lymph. In immunology, the name ascribed to immune mechanisms leading to antibody products.

HYPERTHERMIA Exceptionally high temperatures.

IN UTERO Within the uterus or womb.

IN VITRO Within glass; observable in a test tube.

IN VIVO Within the living body.

INFINITE SLAB A piece of material that has a infinite cross section but finite thickness.

IONIZING ELECTROMAGNETIC RADIATION Electromagnetic radiation of high frequency, short wavelengths, and high photon energy which, when it interacts with matter, causes the removal of electrons from atoms, e.g., x-rays and gamma rays.

KILOHERTZ (KHz) One thousand cycles per second.

LOSSY CAPACITOR A capacitor containing a dielectric material with a loss tangent above 0.1.

MACROMOLECULE A molecule, such as a protein or a nucleic acid, that has a molecular weight greater than a few thousand.

MEGAHERTZ (MHz) One million cycles per second.

METASTABLE A state that is not stable but will exist for a long period of time.

MICROWAVES A particular segment of the RF radiation spectrum with a frequency range of 300 MHz to 300 GHz.

MITOGEN A substance that stimulates lymphocytes to proliferate independently of any specific antigen.

MODULATION The process of varying the amplitude, frequency, or phase of an RF carrier wave.

MULTILAMELLAR VESICLES Phospholipid bilayers that form a series of concentric closed spherical structures somewhat analogous to the layers of an onion; these structures are commonly used as models for studying membrane properties.

MYELOPOIESIS The formation of bone marrow and the cells that arise from it.

NEUROTRANSMITTER A chemical substance that transmits nerve impulses across a synapse.

NEAR FIELD REGION See antenna regions.

NONIONIZING RADIATION (NIR) Electromagnetic radiation of low frequency, long wavelength, and low photon energy, unable to cause ionization (i.e., to remove an electron from an atom); e.g., RF radiation.

NONTHERMAL Not related to heat.

NUCLEIC ACIDS Biochemical compounds, consisting of one or more subrings of a base, a sugar, and a phosphate group. When subrings are covalently bonded to each other, forming a chain, the bond occurs between the sugar and the phosphate, with the base off to the side. In DNA (q.v.), two such chains are weakly attached to each other through contact of their bases, which form the rungs of a ladder, while the sugar and phosphate groups form the sides of the ladder. The bases associate with each other only if their chemical structure is compatible, i.e., complementary. There are four such bases commonly found in DNA. The sequence of these bases provides the information necessary to make other biochemical molecules.

OPERANT CONDITIONING The process of rewards and reinforcements by which specific behaviors are learned.

ORGANOGENESIS The development or growth of organs, especially embryologic.

OSMOTIC FRAGILITY The tendency of a cell membrane to break because of a large imbalance of ion concentration inside and outside the cell.

PARABOLIC REFLECTOR One of the most widely used microwave antennas, consisting of a metal disk whose surface forms a circular parabola.

PARAMETER Any of a set of physical properties whose values determine the characteristics or behavior of something.

PHAGOCYTOSIS The engulfing of microorganisms, other cells, or foreign bodies by phagocytes.

PENIA Reduction in the number of cells; e.g., neutropenia, reduction in the number of polymorphonuclear neutrophiles.

PERITONEAL Relating to the peritoneum, which is the serous sac lining the abdominal cavity and covering most of the viscera therein contained.

PHILIA Increase in number of cells; e.g., neutrophilia, increase in number of neutrophiles.

PHONON A particle of mechanical vibrational (sound) energy.

PHOTON A particle of electromagnetic energy.

PHOSPHOLIPID BILAYER A double-layered sheet of phospholipid molecules arranged so that the hydrophilic (water-liking) part of the molecules associate with water and the hydropholic (water-disliking) part of the molecules associate with each other and avoid contact with water; this structure is the basis for biological membranes.

PLASMID Short piece of DNA that normally codes for one of a few proteins and can often be transferred to another cell; it is usually separate from the cell's major DNA, which carries the information for reproducing the cell.

PLANE WAVE An electromagnetic wave in which the electric and magnetic field vectors lie in a plane perpendicular to the direction of wave propagation.

POIKILOTHERM A cold-blooded animal; an ectotherm; an animal with little or no control of its body temperature.

POLARIZABILITY A linear coefficient that quantitates the change in the magnitude of the dipole moment (q.v.) of a molecule or any other structure in response to an electric field, i.e.,

$$\vec{d} = \alpha\vec{E} + \vec{d}_0$$

where α is the polarizability, $\vec{E}$ is the applied electric field, and $\vec{d}_0$ is the dipole moment when there is no applied field.

POWER DENSITY Magnitude of the Poynting vector at a point in space, in power per unit area (watts per square meter). For plane waves E^2 is simply related to power density, and it is the quantity measured by a survey meter when the sensing element is sensitive to the square of the magnitude of the electric fields; i.e., $P = E^2/3770$, in mW/cm^2.

PROLATE SHPEROID An approximately spherical object that is elongated in the direction of a line joining the poles; similar to a football.

PUPA The second stage in the development of an insect, between the larva and the imago.

RADIATION The transfer of energy from one body to another through an intervening medium.

RADIOFREQUENCY RADIATION See RF radiation.

RESONANCE A small electrical stimulus at a given frequency that produces a large amplitude response in the system at the same frequency.

RESONANT FREQUENCY That frequency which produces resonance in a system; typically those frequencies whose wavelengths are integral multiples of the body's length.

RESPIRATORY CONTROL RATIO A measure of mitochondrial activity and integrity; the rate of utilization of oxygen in the presence of adenosinediphosphate (ADP) divided by the rate of utilization of oxygen in the absence of ADP.

RESTING METABOLIC RATE (RMR) The metabolic rate of an animal which is resting in a thermoneutral environment but not in the postabsorptive state. The relationship of RMR (W/kg) to body mass, M (kg), is $RMR = 3.86M^{-0.24}$. Basal metabolic rate (BMR) is the rate of energy production of an animal in a rested, awake, fasting, and thermoneutral state.

RF RADIATION Radiofrequency radiation; nonionizing electromagnetic radiation in the frequency range 0 to 3000 GHz.

SARCOMA A tumor, usually highly malignant, formed by proliferation of poorly differentiated cells; a malignant connective tissue neoplasm.

SCHEDULE OF REINFORCEMENT Also called reinforcer schedule. The specification of the way in which reinforcers are assigned to particular responses within an operant class or classes. Examples include: the fixed ratio schedule, in which the last of a constant, specified number of responses is reinforced; the fixed interval schedule, in which a constant, specified period of time must elapse before a response is reinforced; the differential reinforcement of low rate schedule, in which a response is reinforced only if at least a specified period of time has elapsed since the last response.

"SILK" Polyester material used in the silk-screen graphic process.

SPECIFIC ABSORPTION The absorbed energy in the tissue, in joules per kilogram (J/kg). See also SPECIFIC ABSORPTION RATE.

SPECIFIC ABSORPTION RATE (SAR) The rate at which energy is absorbed in the tissue, in watts per kilogram: $SAR = \sigma E_t^2/\rho$, where σ = tissue conductivity at irradiation frequency, E_t = rms electric field strength in the tissue, and ρ = tissue density.

SPONTANEOUS BEHAVIOR Unlearned or natural responses to a stimulus.

SQUARE LAW The output of a device is proportional to the square of the input to the device.

SUBSTRATE The molecule upon which an enzyme catalyzes a chemical reaction.

SURVEY INSTRUMENT A portable instrument capable of measuring the strength of electric and magnetic fields.

SYNGENEIC Individuals of a species that are genetically identical at all relevant transplantation loci.

TEMPERATURE-HUMIDITY INDEX A means of estimating the heat stress caused by variations in temperature and humidity.

TERATOLOGY That division of embryology and pathology which deals with abnormal development and congenital malformations.

THERMAL EFFECT In the biological tissue or system, an effect that is related to heating of the tissue through the application of electromagnetic fields, and that can occur through other forms of heating.

THERMOGRAM A recording of temperature distribution over a surface or in a material as measured at the surface.

THERMOGENIC LEVELS Power densities of RF radiation which produce measurable temperature increase in the exposed object.

THERMOGRAPHY A technique for detecting and measuring variations in heat emitted by various regions of the body.

THERMOREGULATION The maintenance of a particular temperature in the living body.

TRANSDUCE To convert one form of energy into another form, e.g., from heat to electrical current in a thermocouple.

TWIN-WELL CALORIMETRY The technique used to determine the absorbed RF dose or dose rate by comparing the excess heat in an RF-exposed system to an identical unexposed system in a comparison well.

VIGILANCE The degree of attentiveness or watchfulness. Vigilance is often investigated by measuring the number of times the occurrence of an infrequent event is correctly detected. In some experiments objective measurements are made of the times the subject looks for occurrence of the infrequent event. Called observing responses, these responses may be required to allow observation of the infrequent event.

WAVE A disturbance that moves through a medium.

WAVEGUIDE A transmission line comprised of a hollow conducting tube within which electromagnetic waves may be propagated.

WAVE, TRANSVERSE ELECTRIC (TE) In a homogeneous, isotropic medium, an electromagnetic wave in which the electric field vector is everywhere perpendicular to the direction of the propagation.

WAVE, TRANSVERSE ELECTROMAGNETIC (TEM) In a homogeneous isotropic medium, an electromagnetic wave in which the electric and the magnetic field vectors are everywhere perpendicular to the direction of propagation.

WAVE, TRANSVERSE MAGNETIC (TM) In a homogeneous isotropic medium, an electromagnetic wave in which the magnetic field vector is everywhere perpendicular to the direction of the propagation.

WAVELENGTH The distance between points of corresponding phase of a periodic wave of two constant cycles. The wavelength λ is related to the phase velocity v and the frequency by $\lambda = v/f$.

WHOLE-BODY IRRADIATION Pertains to the case in which the entire body is exposed to the incident electromagnetic energy or the case in which the cross section (physical area) of the body is smaller than the cross section of the incident radiation beam.